Drug Utilization Review Board

Oklahoma Health Care Authority

4545 N. Lincoln Suite 124

Oklahoma City, Oklahoma 73105

OHCA Board Room

February 8, 2006 @ 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 – February 8, 2005**

DATE: February 2, 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

OHCA Annual Report, Strategic Planning, and Accomplishments

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

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

Medicaid Pharmacy Program Overview and DUR Plus – **See Appendix C.**

Action Item – Vote to Prior Authorize Nasal Allergy Products – **See Appendix D.**

30 Day Notice to Prior Authorize Muscle Relaxants – **See Appendix E.**

Action Item – Annual Review of Hypertensive PBPA Category – **See Appendix F.**

Action Item – Annual Review of Smoking Cessation Products – **See Appendix G.**

Action Item – Annual Review of Growth Hormones – **See Appendix H.**

Fuzeon® Follow Up – **See Appendix I.**

New Product Reviews and Notices – **See Appendix J.**
30 Day Notice to PA Ultram® ER and ODT

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

Future Business

Adjournment

Drug Utilization Review Board

(DUR Board)

Meeting – February 8, 2006 @ 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 Carol McFarland, C.P.A., Dr. Whitsett, Chairman:

3. OHCA Annual Report, Strategic Planning, and Accomplishments

Items to be presented by Dr. Whitsett, Chairman:

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

A. January 11, 2006 DUR Minutes – Vote
B. Provider Correspondence

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

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

A. Retrospective Drug Utilization Review for October 2005
B. Medication Coverage Activity Audit for January 2006
C. Help Desk Activity Audit for January 2006

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

6. Medicaid Pharmacy Program Overview and DUR Plus – See Appendix C.

A. Medicaid Pharmacy Program Overview
B. DUR Plus Overview

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

7. Action Item – Vote to Prior Authorize Nasal Allergy Products – See Appendix D.

A. Product Summary
B. COP Recommendations

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

8. 30 Day Notice to Prior Authorize Muscle Relaxants Products – See Appendix E.

A. Utilization Review
B. COP Recommendations

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

9. Action Item – Annual Review of Hypertensive PBPA Category – See Appendix F.

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

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

10. Action Item – Annual Review of Smoking Cessation Products – 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. Moore, Dr. Whitsett, Chairman:

11. Action Item – Annual Review of Growth Hormones – See Appendix H.

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

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

12. Fuzeon® Follow Up – See Appendix I.

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

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

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

A. 30 Day Notice to Prior Authorize Ultram® ER and Ultram® ODT

14. FDA and DEA Updates – See Appendix K.

15. Future Business

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

16. Adjournment

APPENDIX A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of JANUARY 11, 2006

BOARD MEMBERS:	PRESENT	ABSENT
Brent Bell, D.O., D.Ph.	X	
Dorothy Gourley, D.Ph.	X	
Anetta Harrell, 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: Diane Cain, Justin Logan	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:

Aaron Walker, Schering Plough	Dale Roof, Takeda	Mary Beth Webb, Boehringer Ingelheim
Donna Erwin, Bristol Meyers Squibb	Jim Fowler, Astra Zeneca	Chris Caggino, TAP
Ramona Hannah, Epilepsy Assoc of OK	Kay Rote, OK Mental Health CC	Teresa Peden, NAMI Okla
Mark DeClerk, Lilly	Richard Ponder, J&J	Ron Schnare, Abbott
Steve Higgins, TAP	Beverly Young, Epilepsy Assoc of OK	

PRESENT FOR PUBLIC COMMENT:

Kay Rote, OK Mental Health CC	Agenda Item No. 10
Teresa Peden, NAMI Okla.	Agenda Item No. 10
Ramona Hannah, Epilepsy Assoc of OK	Agenda Item No. 10
Kimberly Williams, Schering Plough	Agenda Item No. 11

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, 2005 DUR Minutes

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

ACTION: MOTION CARRIED.

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

4A: Retrospective Drug Utilization Review Report: September 2005

4B: Medication Coverage Activity Report: December 2005

4C: Help Desk Activity Report: December 2005

4D: Pharmacotherapy Management Report: 2nd Quarter FY06

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

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 5: **30-DAY NOTICE TO PRIOR AUTHORIZE NASAL ALLERGY PRODUCTS**

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

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 6: **60-DAY NOTICE TO PRIOR AUTHORIZE MUSCLE RELAXANTS PRODUCTS**

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

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 7: **ANNUAL REVIEW OF ANTIDEPRESSANTS/SSRIs**

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

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 8: **ANNUAL REVIEW OF ANXIOLYTIC/HYPNOTICS**

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

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 9: **ANNUAL REVIEW OF ADHD PBPA CATEGORY**

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

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 10: **REVIEW AND DISCUSS ANTIEPILEPTIC UTILIZATION**

For Public Comment, Kay Rote: *Thank you very much for the opportunity to talk with you about this particular section. Under the antiepileptic utilizations we have a large number of drugs which are anticonvulsants and what I would like to talk about today is that we represent the Oklahoma Mental Health Consumer Council and particularly with folks who have a bipolar disorder. We have a lot of our folks that use the anticonvulsant medications. We've always had a concern which we've talked to the Board about before with the prior authorization process because it's very difficult for some of our folks. A perfect example for you is that when they talk with their pharmacy or go to get their prescription taken care of and the pharmacist says, well no I*

have to wait on this . . . we have to have a PA process. All the consumer (inaudible) and so there, we have difficulty in navigating that PA system with our folks, but then the other issue that I'd like you to consider is that while you're just discussing this for future reference, if you would look at some of the year-long entries, you are going to be not having the dual eligibles next year but we've also had two years in a row where we have advocated for and received additional monies for mental health medications to be brought into the system and you're going to have a lot of these folks that are dual eligible because of their various disabilities, not just necessarily because of age. And so that's going to be reducing your utilization. Some of that utilization was increased because of the additional medications that had to be brought out, so what we're asking is that you might take another year to look at this before you do the prior authorization process because we feel like there's going to be a large number of changes on these particular types of drugs and we have a system in place where we are educating the consumers now on better medication management. And since we have so many that are involved with the anticonvulsants, then that is one area that we would like to take and take special care with to educate them on as far as medication management, so we would like to make you aware of those issues and then as that you take a little bit of time to look at how that usage is done over the next year before we go into this type of process. And the Consumer Council thanks you. Any questions?

For Public Comment, Teresa Peden: *I am Teresa Peden with the National Alliance of Mental Illness here in Oklahoma. I understand that prior authorization for antiepileptics may be under consideration for a future meeting and the National Alliance on Mental Illness has closely monitored the implementation of pharmacy management programs across the country. Other states that have imposed restrictive preferred drug lists and prior authorization requirements in their State Medicaid programs must have recognized that these types of restrictive policies are inappropriate for beneficiaries with mental illnesses and elected to exempt such beneficiaries from restrictive preferred drug lists and prior authorization requirements. States have also required that individuals with mental illnesses who are successfully being treated by non-preferred medications be grandfathered so that they may continue to receive those therapies. NAMI Oklahoma urges you to adopt similar approaches and it is our hope that as you consider prior authorization, you will choose to protect antiepileptics from these restrictions. And NAMI Oklahoma thanks you for the opportunity to present.*

For Public Comment, Ramona Hannah: *My name is Ramona Hannah and I brought an associate with me, Beverly Young. We are with the Epilepsy Association of Oklahoma. We are very concerned that antiepileptic medications would be in a category of prior authorization or any tier that I've been seeing here tonight . . . tiers. I've made notes since I don't have a thing for the screen and what I'd like to do is just read a brief note. It's just about a one moment, but I've made copies and I've attached to these notes a letter, just a little more wordy, and if I may after I speak, pass each of you this and take home and read it . . . is that going to work? Okay. Access to all medications a doctor has prescribed is a critical issue for people who have seizures. There are more than twenty different kinds of seizure medications. Also that many seizure types. These medications are not interchangeable, but indicated for a particular seizure type. The volunteers of the Epilepsy Association talk daily with people with epilepsy. We know some have tried several medicines before finding one that is tolerable and effective. Getting the medicines is then complicated by lack of money, no insurance or insurance restrictions such as prior authorizations, formularies, tiers, or required generics. Those of us who have personal experience, and both my associate and myself both have family members with epilepsy as well as our work with the Epilepsy Association, and we've had personal experience with family members . . . know that a change of medication has resulted in a trip to the emergency room or resulted in a car wreck because breakthrough seizures can happen so easy with a change of medication. We oppose a prior authorization restriction be put on antiepileptic medication. This classification of medicines is too specialized to be substituted and should not even be considered for anything but as the doctor prescribes. I thank you and if I may, just take one and pass it back.*

Dr. Bell: *Teresa, what states did you look at specifically that you . . .*

Teresa Peden: *Actually what I did was I went onto the NAMI website and also I talked with some of the National Alliance people about it and that's where I got my facts because they've done all the national . . .*

Dr. Bell: *So it's on the NAMI website?*

Teresa Peden: *Yeah, there's some specific information on the NAMI website.*

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

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 11: NEW PRODUCT REVIEWS AND NOTICES

For Public Comment, Kimberly Williams: *Good evening. I want to thank you for giving me time to speak about Asmanex®. I just want to briefly give you an overview of a new inhaled corticosteroid that was approved in March '05. I'm sure you all know these facts; I'm just going to reiterate them because it's asthma. Asthma ranks as one of the most common conditions in the United States. Approximately 30 million Americans suffer from asthma and approximately 12 million have attacks or episodes each year and there are still four to five thousand deaths per year, asthma related deaths, which is still too many for a chronic condition that can be controlled with medication that is out on the market today. And according to the 2002 estimates, the indirect and direct costs of asthma totaled $14 billion, and hospital care was a huge chunk of that cost. It mainly may be due to compliance. These patients are not taking their inhaled corticosteroids or beta agonists like they should. Based on the current guidelines on how corticosteroids are the cornerstone of asthma therapy and they're recommended as first line for treatments in mild, moderate and severe asthma, and (unintelligible) corticosteroids have shown to be the most effective long term maintenance treatment medication for asthma. They reduce hyper responsiveness, improve peak expiratory flow rate, reduce symptoms and prevent exacerbations. So again, Asmanex® is an inhaled corticosteroid. It was approved for the treatment of asthma in March '05 for patients 12 years and older. Currently it is the only inhaled corticosteroid that is FDA approved for once daily administration at initiation and for maintenance treatments of asthma. It is shown to be effective and have a therapeutic benefit for over 24 hours. So there were several studies, 12-week double blind placebo controlled trials that were conducted for the registration of Asmanex® for the approved doses of 220 mcg once a day in the evening, 440 once a day in the evening and 440 twice daily. And these doses are based on asthma severity. These trials examined the whole spectrum of asthma patients. The first group of trials were conducted in steroid (unintelligible) patients using only short acting beta agonists. And*

these studies show an improvement in the primary variables that you look at when you're evaluating asthma improvement. FEV_1 (unintelligible) peak expiratory flow rate and decrease in albuterol use. And these particular patients you saw decreasing about half of the use of the albuterol for the day. The second group of studies were conducted on patients who were previously on inhaled corticosteroids that were currently on the market. And these studies also showed that patients who received Asmanex® had a significant improvement in FEV_1, a.m. peak expiratory flow rate, daytime and nighttime symptoms, and a decrease in albuterol use as well. And lastly, there was a study conducted using the oral corticosteroid dependent patients, and these studies, the patients were able to decrease their prednisone dose by almost half, and in addition, 40% of the patients were able to eliminate the use of prednisones altogether. So all the clinical trials show that Asmanex® was safe, it's a low total bioavailability, so that any amount that's swallowed is rapidly degraded via first path metabolism. Asmanex® is highly protein bound and no active metabolites that would contribute to systemic side effects and at recommended doses, Asmanex® has shown no suppression of the HPA axis. And side effects overall were relatively mild and none required the discontinuation of the product. And to conclude, Asmanex® may help contribute to or better compliance. And the reason being is it can be dosed once a day. And compliance is a huge issue with this population, so it can be used, dosed once a day. The device is easy to use. You twist the cap, you inhale and you put the cap back on. And actually twisting the cap loads the dose. And each actuation is 220 mcg. And the actual delivery dose is 200 mcg. And also with the device is independent of inspiratory flow rate, so those patients who are one the emphysema side, about 30 mls per minute, versus those who are mild asthmatics, you're going to get a consistent dose no matter how you inspire which is important. It also has a dosage counter that counts down each time the patient takes a dose so it lets the patients and the caregivers know how much drug is remaining in the device. And lastly, once all the doses have been used, the device actually locks to prevent patients from trying to inhale and there's no medication in the device. That's my brief overview. Any questions:

Dr. Whitsett: *Yes . . . I'm a little unclear about the delivery of this unrelated to flow rate because I can imagine that sort of goes against what I've always thought about delivering inhaled products.*

Kimberly Williams: *Okay. Well let me, one thing it's a dry powder inhaler. I hope I said that at the beginning. It is a dry powder inhaler. And what I mean independent is that the dose is consistent. So some inhalers, if you don't inspire heavily enough, you won't get the consistent dose that's actually, that you're supposed to be getting as said on the package. So that's what I mean by independent . . .*

Dr. Whitsett: *So it's a dry powder that you have a very reduced inhalation flow rate, then is it not going to have more contact with oropharangeal mucous membranes and upper airway, rather than getting to where your target organ receptors are?*

Kimberly Williams: *Well, depending, one . . . the particle size helps, having the smaller particle size, which this has respirable particle sizes that are less than about 4 microns, so that helps. And I would imagine that if you inspire less than normal you may have the chance of depositing more in the oropharans. But because the particles are so small, in general it can be inspired even if you're at about 30 mls per minute. Thank you very much.*

Materials included in agenda packet; presented by Dr. 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: Contraceptive Utilization Review
13B: Antidiabetic Utilization Review
13C: Antiinfectives Utilization Review
13D: Analgesic/Narcotic Utilization Review
13E: Annual Reviews
13F: New Product Reviews
13G: OTC Formulary

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

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 14: ADJOURNMENT

The meeting was declared adjourned.

ACCREDO
THERAPEUTICS™

January 30, 2006

DUR Board
Oklahoma Health Care Authority
4545 N. Lincoln Blvd.
Suite 124
Oklahoma City, OK 73105

To Whom It May Concern:

I am enclosing two letters sent by Endocrinologists clarifying their thoughts of the use of bone age in the diagnosis of disorders for Growth Hormone therapies. I had requested these letters be sent to me since I am the liaison in regards to submitting the authorization requests for their patients and that is why Dr. Kemp had addressed his to my attention. I would like to request that these letters be put into your DUR packet for review for your February 8, 2006 meeting. Thank you for your time and consideration in this matter.

Sincerely,

Lori Bickford
Senior Clearance Specialist
Accredo Therapeutics
4901 W. Reno Avenue
Ste. 950
Oklahoma City, OK 73127

UAMS
COLLEGE OF MEDICINE
DEPARTMENT OF PEDIATRICS
UNIVERSITY OF ARKANSAS FOR MEDICAL SCIENCES

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Accredo Therapeutics
4901 W. Reno Avenue Ste. 950
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Pediatric Endocrinology
Arkansas Children's Hospital

800 Marshall St., Slot 512-3
Little Rock, AR 72202-3591

Telephone: 501-364-1430
Fax: 501-364-6299
Toll-Free: 800-495-1048

Dear Lori,

In reference to your question as to using bone ages as a criterion for the diagnosis of growth hormone deficiency, I would offer the following thoughts:

1. It is important to include bone age as part of the work up for GHD. The reason for this determination is three-fold. First, a significant bone age delay is an indication of pathology and encourages a more aggressive work-up to determine the cause of the growth delay. Second, bone age is a good way to estimate growth potential. Third, it is important to be certain that epiphyses are still open before contemplating therapy with growth hormone.

2. There are some problems, however, in using bone age as a criterion as to whether one should require a bone age delay before using growth hormone. One problem is that bone ages are not actually quantitative. They are more or an estimate, and have a wide standard deviation (about 1 year, although it varies with age, being even larger during puberty). The other issue is that the bone age is not universally delayed with growth hormone deficiency. For example, a child with acquired GHD (for example, someone who has been treated for a craniopharyngioma) may not have been deficient in growth hormone for a period of time sufficient to cause delay in the bone age. Another issue is that the less the bone age delay, the more the urgency to begin treatment, since if there is no bone age delay there is less potential time for therapy until epiphyseal closure.

In conclusion, I believe that it is important to determine bone age as part of the work up of short stature, but that to include it as a criterion for making the diagnosis of growth hormone deficiency or deciding whether to treat with growth hormone is asking more of this determination than is appropriate (except for ascertaining that the epiphyses are sufficiently open to respond to growth hormone).

Sincerely,

Stephen F. Kemp, M.D., Ph.D.
Professor of Pediatrics
President, Human Growth Foundation

Original

David B. Domek, M.D.

Pediatric Endocrinology, Genetics & Metabolism
Board Certified in Pediatrics and Medical Genetics

January 26, 2006

Oklahoma Health Care Authority
4545 N. Lincoln Blvd.
Suite 124
Oklahoma City, OK 73105

To Whom It May Concern:

It has come to my attention that bone age criteria are being used as a diagnostic component for GHD. In my opinion, bone age delay is not a necessity for the diagnosis for GHD, but rather a reflection of the underlying pathology. Bone age delay is usually associated with GHD, but also is present commonly in normal variations. To make it a necessity for diagnosis would penalize those children diagnosed early.

The accurate diagnosis of GHD requires data from a variety of sources; auxologic biochemical and radiographic. Some carry more weight than others. A bone age delay may in some way signify the length of deficiency and may predict the length of therapy, but is not a necessity for diagnosis.

Sincerely,

David B Domek MD

David B. Domek, MD
DBD/sjd

3366 N.W. Expressway, Ste. 330 • Oklahoma City, Oklahoma 73112
405-945-4525 • Fax (405) 945-4535

Original Fax

APPENDIX B

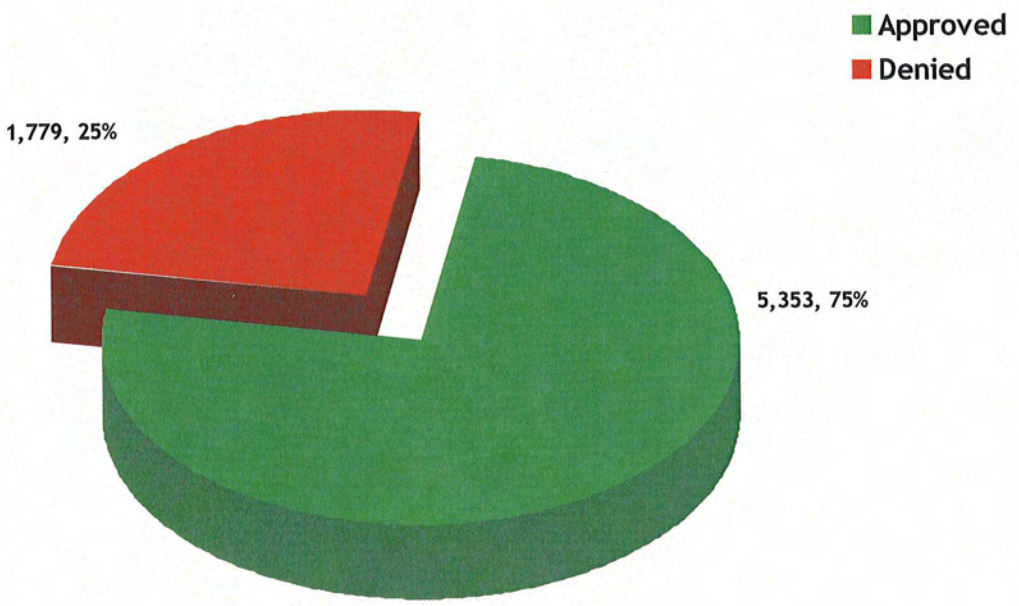
Retrospective Drug Utilization Review Report

Claims Reviewed for October 2005

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Total # of messages returned by system when no limits were applied	112,859	110,973	1,097,461	50,586
Limits which were applied	Established, Major, Males 50-65	Acetamenophen, Females, Age 22-26, abuse and no abuse potential	Contraindicated, age 22-35, with Asthma	High dose, Digitalis, Males and Females, Age 0-65
Total # of messages after limits were applied	65	170	14	24
Total # of clients reviewed after limits were applied	65	152	11	23

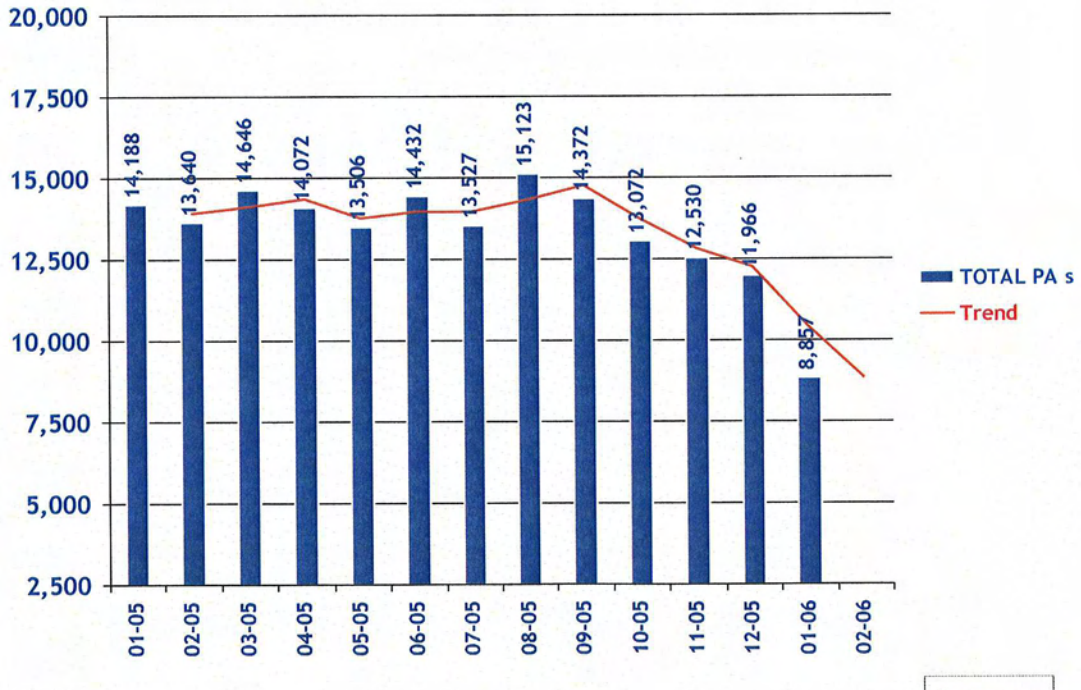
LETTERS			
Prescribers		**Pharmacies**	
Sent	**Responded**	**Sent**	**Responded**
185		134	

PRIOR AUTHORIZATION ACTIVITY REPORT
January 2006



PHARMACY Management Consultants

PRIOR AUTHORIZATION REPORT
January 2005 - January 2006



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Activity Audit for

January 01 2006 Through January 31 2006

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.	12		2295		909		24		678		37		11		3		34		208		3		143		
Den.		8		389		405		0		171		106		16		0		46		21		2		115	
Average Length of Approvals in Days	18		92		93		159		194		244		179		123		296		291		33		201		

Changes to existing PA's	685
Total (Previous Year)	14188

* Denial Codes	
762 = Lack of clinical information	24.28%
763 = Medication not eligible	1.85%
764 = Existing PA	1.24%
772 = Not qualified for requested Tier	5.40%
773 = Requested override not approved	14.78%

SUPER PA's	
Admitted to Nursing Home	24
Early Refill Attempts	25506
Dosing Change	313
High Dose	9
Lost/Broken Rx	90
Stolen	6
Other	37
Wrong D.S. on Previous Rx	13
Quantity vs. Days Supply	1051
Brand	108
-- Approved	39
-- Denied	19

Monthly Totals

	Number	Percent of Total
Approved	5238	59.14%
Additional PA's	15	0.17%
Emergency PA's	0	0.00%
Duplicates	407	4.60%
Incompletes	1418	16.01%
Denied *	1779	20.09%
Total	8857	100.00%

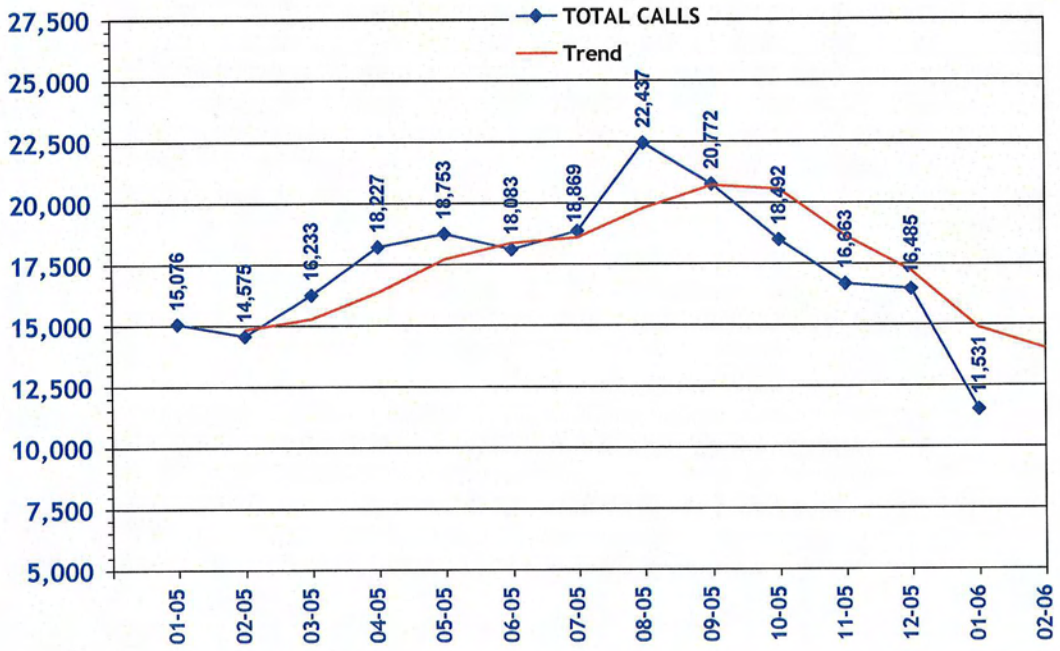
Daily Average of 402.59 for 22 Days

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
January 2005 - January 2006



PHARMACY Management Consultants

APPENDIX C

Oklahoma Medicaid Pharmacy Overview and DUR Plus

February 2006

Medicaid Pharmacy Program Background

Medicaid was enacted in 1965 as a program designed to provide health care to low income individuals who received cash assistance payments from the government. Since that time, it has been expanded to include individuals with disabilities and those in long term care facilities.

Forty years ago, prescription drugs were not included in the list of mandatory services that states must provide in order to receive federal financial participation for the Medicaid program. Today, in spite of the prevalence of pharmaceutical care and the apparent benefits which can be derived from them, drug coverage is still optional under state Medicaid plans. However, all states currently provide a pharmacy benefit for their Medicaid recipients because of the evidence supporting the use of prescription drugs for treatment and prevention of illness, disease, and complications.

Until 1991, states had little incentive to provide prescription drugs to their Medicaid recipients. Many states, including Oklahoma, provided a very limited pharmacy benefit for clients, covering such things as heart and blood pressure medications, cancer chemotherapy, pain relievers, and antibiotics. The Omnibus Budget Reconciliation Act of 1990 (OBRA 90) changed all that by setting requirements for Medicaid pharmacy programs and tying those requirements to a drug rebate program with pharmaceutical manufacturers.

The Medicaid Drug Rebate Program guarantees that the Medicaid program was given the "best price" for all pharmaceutical products. In exchange for this best price, Medicaid programs would be required to cover all drugs of participating manufacturers. The exception to this requirement includes drugs in the following therapeutic categories:

1) Drugs for weight loss or weight gain
2) Fertility
3) Cosmetic or hair growth
4) Symptomatic relief of cough and colds
5) Smoking cessation
6) Prescription vitamins and minerals, other than prenatal preparations and fluoride
7) Barbiturates
8) Benzodiazepines

All states currently cover at least some of these drugs. Oklahoma Medicaid covers both prescription and non-prescription products used to assist clients with

tobacco cessation and covers barbiturates and benzodiazepines for treatment of seizures and behavioral health conditions.

Over the past 15 years since OBRA 90 took effect, Medicaid pharmacy programs have been through a series of changes. Although states are free to design their own benefit structures, many of the programs implement similar measures to ensure that medications are used appropriately.

Prior authorization programs are used in Medicaid programs as well as in commercial health plans. These programs have frequently been chastised as looking only at the cost of a particular medication and not at the benefit provided by the drug therapy. The task of the Oklahoma DUR Board is to balance the need for the medication with the potential for inappropriate use.

In 2000, Oklahoma implemented one of the first preferred drug programs in the nation. Although we call it the Product Based Prior Authorization (PBPA), it is a forerunner to the current Preferred Drug List (PDL) programs which are prevalent in pharmacy benefit designs. The categories included in the PBPA are listed below:

Anti-Ulcer
NSAIDs
ACE Inhibitors
ARBs
Calcium Channel Blockers
ADHD/Narcolepsy Treatment
Antidepressants
Statins
Fenofibrate
Bladder Control

For each of these categories, the DUR Board has designated first and second tier drugs. First tier drugs are available without prior authorization. Second tier drugs require the use of a first tier drug in a step therapy protocol or a prior authorization. Each category has unique clinical criteria for the approved use of a Tier 2 product.

As an extension of the PBPA, in 2004, OHCA began offering an opportunity to participate in Supplemental Rebates as a way for pharmaceutical manufacturers to make their Tier 2 products more cost-effective and remove the prior authorization requirement. Currently we have manufacturers participating in most of the categories listed above.

Before the PBPA program was implemented, OHCA used prior authorizations based on scope and/or utilization. Currently we have several single drug

products in this type of program, as well as several drug categories, such as the non-sedating antihistamines, benzodiazepines, and smoking cessation products.

All drugs which are subject to prior authorization must be reviewed at least annually according to state law. These reviews are spread out over the year, but typically there is a concentration of these reviews in the first few months of the year.

Other utilization programs include quantity limits, age or sex restriction, days supply limits and Prospective Drug Utilization Review edits. These edits will alert the pharmacy to situations of potential danger to the client including drug-drug interaction, drug-disease interaction, early refill, and high dose warnings.

The monthly prescription limit for adults in Oklahoma Medicaid is capped at six, and of those, up to three may be brand name drugs. Children up to age 21 are not subject to a monthly prescription limit. Adults in long term care settings are also not limited. Clients who are eligible for one of the Home and Community Based Waiver programs have the six regular prescriptions, plus seven extra generics. For HCBW clients who require more than three branded drugs or more than thirteen total drugs per month, there is a program called Pharmacotherapy Management which reviews their medications and checks for duplicate therapy, contraindicated therapy, or ways to consolidate treatment. If the review determines that there is medical necessity for the additional drug products, prior authorizations can be granted.

With the implementation in January of the Medicare Part D pharmacy benefit, approximately 80,000 Medicaid clients will no longer receive their prescriptions through the Medicaid program. Although they represent only about 15% of the Medicaid population, their pharmacy spending represents 45-50% of total drug spend. The clients who are eligible for the new Medicare Part D benefit include most of the elderly who reside in long term care facilities and many of the disabled adults who participate in the HCBW programs.

DUR PLUS

Medicare Part D provides OHCA with an opportunity to streamline some of the prior authorization processes by automating the approval process. Several states have been using an application which is integrated into their claims processing system. Because OHCA has not only pharmacy claims, but also medical and hospital claims, the system can be configured to search for diagnosis codes, procedure codes, level of care, and previous medication usage to determine whether a prior authorization should be approved.

EDS, the OHCA claims processing contractor, has developed an application called DUR Plus which incorporates these prior authorization determinations into

the claims processor. This eliminates the need for paper authorization forms to be faxed to and from pharmacies and physicians offices. For some prior authorizations, the documentation requirement will dictate that the authorization request be handled as it is currently, but a large number of the requests can be handled electronically.

In addition to the PA processing, DUR Plus will integrate ProDUR edits, quantity limits, age and gender restrictions, total daily dose calculations, and other features that are not currently available in the OHCA claims processing system. DUR Plus is tentatively scheduled to be implemented in January 2007.

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APPENDIX D

Vote to Prior Authorize Nasal Anti-Allergic Products

Oklahoma Medicaid
February 2006

Available Nasal Products

Anticholinergics: This category is most effective for treatment of severe vasomotor symptoms. Ipratropium bromide 0.03% is approved for symptomatic relief of rhinorrhea associated with allergic and non-allergic perennial rhinitis in adults and children 6 years of age and over, while the 0.06% is approved for symptomatic relief of rhinorrhea associated with the common cold for adults and children 12 years of age and over (and its safety for greater than 4 days has not been established). The most frequently reported adverse events are epistaxis and nasal dryness.

Antihistamines: Azelastine is approved for treatment of the symptoms of seasonal allergic rhinitis in children 5 years of age and over and for treatment of the symptoms of vasomotor rhinitis in adults and children 12 years of age and over. The primary adverse effects were altered taste and nasal burning.

Corticosteroids: These agents are the most effective agents for treating allergic rhinitis and are considered first line therapy. Regular use is required for maximum benefit. These products are generally well tolerated. The most common side effects include sneezing, stinging, and local irritation. The aqueous formulations may be preferred as they are less irritating.

* Approved for children 3 years of age and over: Mometasone furoate (Nasonex).
* Approved for children 4 years of age and over: Fluticasone (Flonase).
* Approved for children 6 years of age and over. Beclomethasone (Beconase, Vancenase), Flunisolide (Nasarel), Budesonide (Rhinocort), and Triamcinolone (Nasacort).

Recommendation

The College of Pharmacy recommends the addition of the Nasal Allergy 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.

Nasal Allergy Products	
Tier-1*	***Tier-2***
Flonase® flunisolide Ipratropium bromide	Nasonex® Beconase® AQ 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-1 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.

APPENDIX E

30 Day Notice to Prior Authorize Skeletal Muscle Relaxants

Oklahoma Medicaid

February 2006

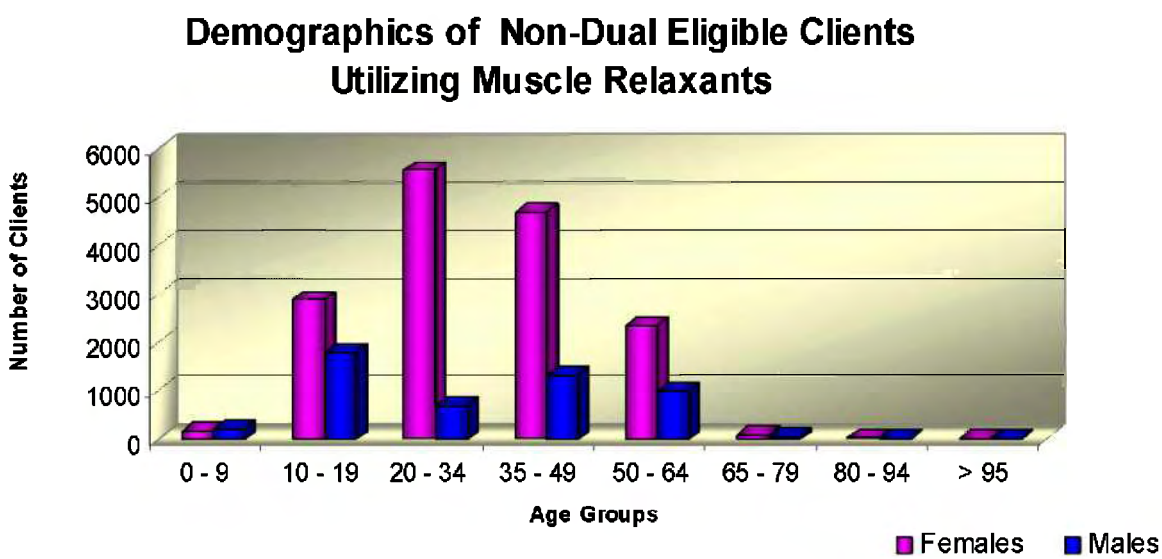
Place in Therapy of Skeletal Muscle Relaxants

The recommended treatments for musculoskeletal conditions 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 and 90% of these cases resolve with proper care and rest in about 4-6 weeks.

Oral skeletal muscle relaxants can be effective when used for acute symptomatic relief of pain and discomfort, but there is little evidence to support the use of skeletal muscle relaxants for chronic pain. There is a lack of high quality studies to suggest that any skeletal muscle relaxant is more efficacious than the other.[1] Most clinical trials of skeletal muscle relaxants are 2-3 weeks in duration and seldom continue beyond 6 weeks[2]. Some trials show a decline in efficacy to rates similar to that of placebo after 4-7 days.[3,4,5,6] As such, these agents are only recommended for short-term use.

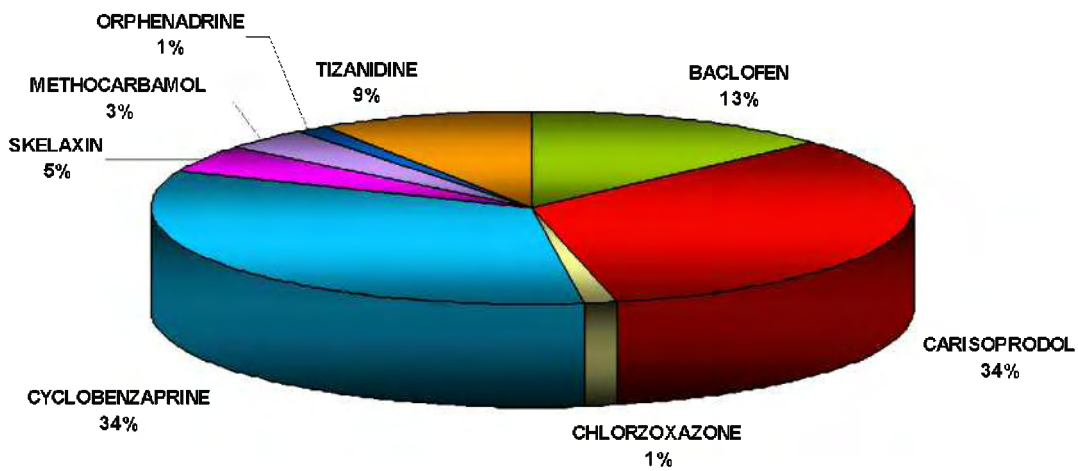
Utilization of Skeletal Muscle Relaxants

The following table shows the demographics of the clients utilizing skeletal muscle relaxants. It is evident that the client demographics are not consistent with the disease and epidemiology. Musculoskeletal conditions are more common in the elderly who may have natural wearing or degeneration of the vertebrae and/or surrounding tissue. Sprains and strains are also prevalent in working age adults who may have jobs that require the individual to perform repetitive straining or lifting.



Among the skeletal muscle relaxants prescribed, carisoprodol accounted for almost one third of all the agents used. This is not consistent with current recommendations and research which suggests that use of carisoprodol is generally not recommended due to its unclear benefit profile versus its adverse effect profile. In addition, carisoprodol is metabolized to meprobamate, a sedative-hypnotic with highly addictive properties.

Marketshare by Therapy Days of Non-Dual Eligible Clients Utilizing Muscle Relaxants

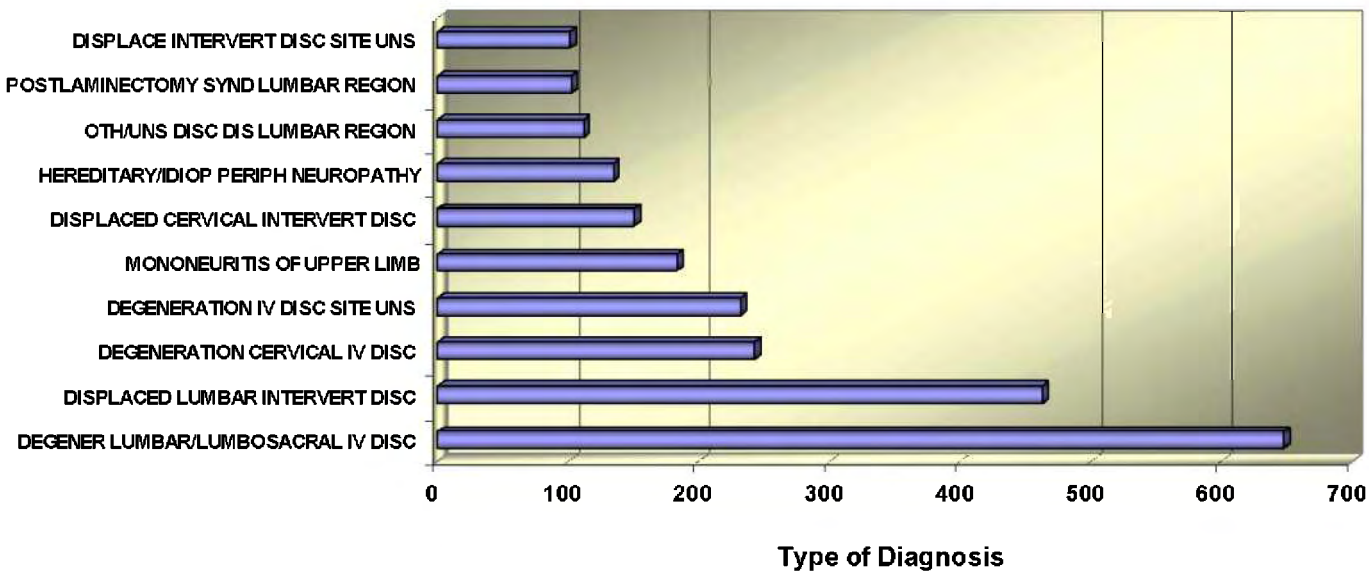


A diagnosis search was conducted for all medical/hospital claims of non-dual eligible clients who had received carisoprodol during fiscal year 2005. A total of 3,850 clients yielded 132,891 diagnoses. However, only 1,592 clients had one of the following diagnoses of interest:

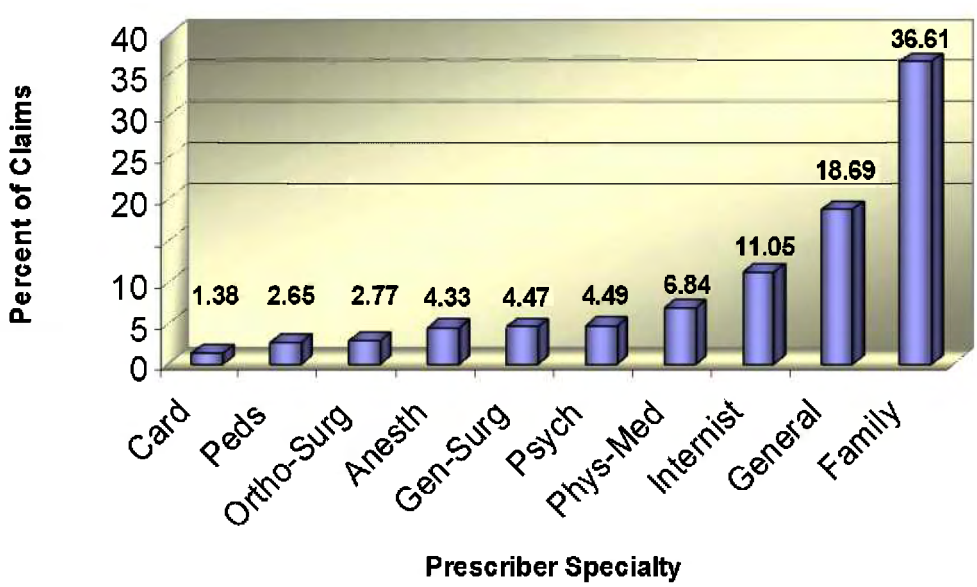
Diagnosis	*Description*	*Frequency*
352	Disorders of other Cranial Nerves	1
358	Myoneural Disorders	3
359	Muscular Dystrophies	13
351	Facial Nerve Disorders	16
350	**Trigeminal Nerve Disorder**	**19**
336	**Other Diseases of Spinal Cord**	**23**
349	**Oth/Unspec Nervous System Disorders**	**29**
340	**Multiple Sclerosis**	**36**
343	Infantile Cerebral Palsy	36
353	Nerve Root and Plexus Disorders	39
342	Hemiplegia and Hemiparesis	69
337	Disease of Autonomic Nervous System	77
357	**Inflammatory and Toxic Neuropathy**	**85**
344	**Other Paralytic Syndromes**	**141**
356	**Hereditary/Idiopathic Peripheral Neuropathy**	**148**
355	**Mononeuritis of Lower Limb**	**183**
354	Mononeuritis of Upper Limb	262
722	Intervertebral Disc Disorders	2,475

The following tables show the top 10 specific diagnosis of non-dual eligible clients utilizing carisoprodol and the prescribers of carisoprodol in this population. Out of 3,850 clients who received carisoprodol, more than half of the clients (2,258) did not have a current relevant diagnosis. Carisoprodol, within its own class, is not a preferred medication, and is not often prescribed off-label for non-approved indications.

Top 10 Specific Diagnoses of Non-Dual Eligible Clients Utilizing Carisoprodol



Top 10 Prescribers of Carisoprodol for Non-Dual Eligible Clients



Carisoprodol

Carisoprodol's only indication is for disease of musculoskeletal conditions. The exact mechanism of action of carisoprodol is not known, but the drug is thought to act by causing sedation rather than exerting direct skeletal muscle relaxation. Once absorbed, carisoprodol undergoes hepatic biotransformation by the cytochrome P450 enzyme 2C19 to hydroxyl-carisoprodol, hydroxylmeprobamate, and meprobamate. The half-life of the parent drug carisoprodol is approximately 1.5 hours, and 8-16 hours or longer for meprobamate.

Meprobamate, an active metabolite of carisoprodol, is a sedative hypnotic classified as a schedule IV drug in the United States. It was once popular in the 1950s until it was replaced by the benzodiazepines due to safety and adverse effect concerns. Carisoprodol is not a scheduled drug at the federal level, which may lead prescribers to undermine the abuse and addictive potential of this medication. In regular users of carisoprodol, it is meprobamate rather than carisoprodol that accumulates.[7] Carisoprodol has been made a scheduled medication in Oklahoma due to abuse concerns.

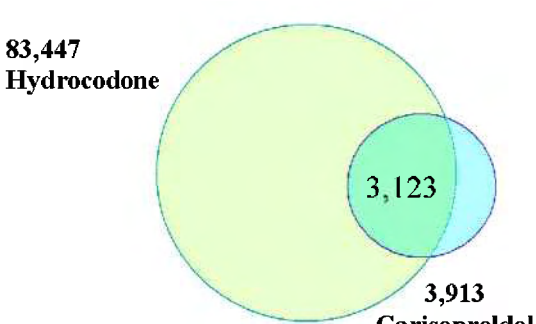
Soma® was initially thought to possess no withdrawal side effects. Studies in dogs showed no withdrawal symptoms occurred after abrupt cessation of carisoprodol. However, recent studies and case reports have indicated that, in humans, withdrawal symptoms occur and may often include back pain or related symptoms, headache, insomnia, and irritability or change in mood.[8,9] Severe withdrawal symptoms from meprobamate have been reported and include symptoms such as hallucinations, agitation, and seizures.

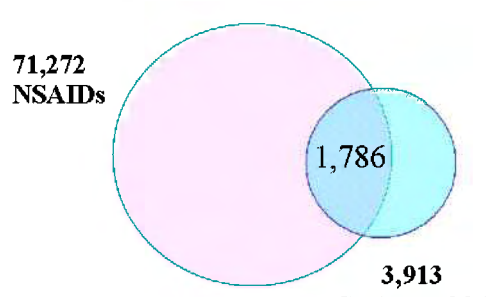
Carisoprodol was ranked 54th among 234 drugs that have abuse potential.[10] Carisoprodol is known to potentiate the sedating and euphoria-inducing properties of alcohol as well as other drugs of abuse. It is also a much cheaper substitute for legally prohibited drugs. As a result, its use has become rampant among patients with a history of substance abuse.[11]

The 2004 report from the American Association of Poison Control Centers[12] included over 8,300 cases regarding carisoprodol intoxication. 6,706 of these cases had to be treated in a healthcare facility with over 400 cases resulting in a major outcome, and 29 cases resulting in death. These numbers were the highest among the class of skeletal muscle relaxants and do not include cases in which carisoprodol was used concomitantly with another agent.

Carisoprodol Utilization with Hydrocodone and NSAIDs

In the Medicaid non-dual eligible population that utilized carisoprodol, 80% of the clients that had a paid claim for carisoprodol during fiscal year 2005 also had a paid claim for a hydrocodone product. The same client database of non-dual eligible clients utilizing carisoprodol was merged with a database of clients utilizing NSAIDs. Only 45% of the carisoprodol utilizers had a paid claim for an NSAID, the first line recommended therapy.





Conclusions and Recommendations

The misuse of any medication has potential negative effects which may lead to overall increase in utilization of healthcare resources, increase hospitalizations, lead to permanent disability, and can even result in death of the affected individual.

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 approval before referral to the Oklahoma Healthcare Authority for final limitations or additions based on cost and clinical effectiveness.

Skeletal Muscle Relaxants

*Tier-1**	*Tier-2*
Cyclobenzaprine (Flexeril®)	Carisoprodol (Soma®)
Baclofen (Lioresal®)	Metaxolone (Skelaxin®)
Tizanidine (Zanaflex®)	
Methocarbamol (Robaxin®)	
Chlorzoxazone (Parafon Forte®, Paraflex®)	
Orphenadrine (Norflex®)	

*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. Approved indication.
2. Documented adverse effect or contraindication to the preferred products.
3. Failure with at least two Tier-1 medications defined as no beneficial response after at least two weeks of use during which time the drug has been titrated to the recommended dose.
4. Approvals will be for the duration of three months, except for clients with chronic diseases such as multiple sclerosis, cerebral palsy, muscular dystrophy, and paralysis, in which case authorizations will be for the duration of one year.

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[1] **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.*

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[4] Basmajian JV: **Acute back pain and spasm: A controlled multicenter trial of combined analgesic and antispasm agents.** Spine. 1989;14:438-9.

[5] Fryda-Kaurimsky Z, Muller-Fassbender H. **Tizanidine in the treatment of acute paravertebral muscle spasm: a controlled trial comparing tizanidine and diazepam.** J int Med Res 1981;9:501-5.

[6] Basmajian JV. **Cyclobenzaprine hcl effect on skeletal muscle spasm in the lumbar region and neck: Two double-blind controlled clinical and laboratory studies.** Arch Phsy Med Rehabil 1978;59:58-63.

[7] Bramness JG, Skurtveit S, Morland J. **Impairment due to intake of carisoprodol.** Drug Alcohol Depend 2004;74:311-8.

[8] Reeves RR, Parker JD. **Somatic dysfunction during carisoprdol cessation: Evidence for a carisoprodol withdrawal syndrome.** JAOA. 103(2) February 2003.

[9] Littrell RA, Sage T, Miller W. **Meprobamate dependence secondary to carisoprodol (Soma) use.** Am J Drug Alcohol Abuse 1993;19:133-4.

[10] Elder NC. **Abuse of skeletal muscle relaxants.** Am Fam Physician 1991;44:1223-6.

[11] Rohatgi G. Rissmiller DJ. Gorman JM. **Treatment of carisoprodol dependence: a case report.** *Journal of Psychiatric Practice. 11(5):347-52, 2005 Sep.*

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APPENDIX F

Antihypertensive Drugs Annual Review - Fiscal Year 2005
Oklahoma Medicaid
February 2006

Product Based Prior Authorization – Antihypertensives

Six 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)
- Angiotensin Receptor Blockers (ARBs) during FY 2005
- ACEI/HCTZ combination drugs
- ACEI/CCB combination drugs
- ARB/HCTZ combinations during FY 2005

Criteria for Authorization

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

- 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

Utilization

For the period of July 2004 through June 2005, a total of 53,386 clients received antihypertensive drugs from the PBPA categories through the Medicaid fee-for-service program.

Utilization Trends of Antihypertensives

	Fiscal Year 2004	*Fiscal Year 2005*	*Percent Change*	
Total Clients	41,075	53,386	Increased	29.9 %
Total Claims	237,576	344,071	Increased	44.8 %
Total Cost	$9,093,828.34	$14,568,988.06	Increased	60.2 %
Total Days	9,681,912	14,038,494	Increased	45.0 %
Per Diem	$0.94	$1.04	Increased	10.6 %

Comparison of Cost vs. Claims between Antihypertensive Classes

Class	*Cost*	*% Cost*	*Claims*	*% Claims*
CCBs	$5,767,535.81	39.6	102,692	29.8
ACEIs	$2,379,198.31	16.3	154,614	44.9
ARBs	$2,815,829.24	19.3	35,884	10.4
ACEI/HCTZ Combinations	$304,467.91	2.1	17,303	5.0
ACEI/CCB Combinations	$1,303,376.53	8.9	11,549	3.4
ARB/HCTZ Combinations	$1,998,580.26	13.7	22,029	6.4
Totals	$14,568,988.06	100.0	344,071	100.0

Calcium Channel Blockers

		Clients	Claims	Units	Days	Cost	Cost/Unit	Cost/Day
Tier 1	**FY 2005**	**15,391**	**77,115**	**3,880,526**	**3,110,527**	**$3,658,563.09**	**$0.94**	**$1.18**
	FY 2004	13,604	64,441	3,239,352	2,649,721	$3,075,846.59	$0.95	$1.16
Tier 2	**FY 2005**	**4,847**	**25,577**	**1,181,594**	**1,077,573**	**$2,108,972.72**	**$1.78**	**$1.96**
	FY 2004	5,582	28,138	1,333,296	1,197,262	$2,254,994.04	$1.69	$1.88

ACE Inhibitors

		Clients	Claims	Units	Days	Cost	Cost/Unit	Cost/Day
Tier 1	**FY 2005**	**28,167**	**146,582**	**7,270,229**	**5,746,608**	**$1,790,978.51**	**$0.25**	**$0.31**
	FY 2004	22,698	108,024	5,491,337	4,225,346	1,547,901.90	$0.28	$0.37
Tier 2	**FY 2005**	**1,529**	**8,032**	**407,830**	**341,908**	**$588,219.80**	**$1.44**	**$1.72**
	FY 2004	3,151	15,123	787,927	648,993	$940,509.69	$1.19	$1.45

ARBs

		Clients	Claims	Units	Days	Cost	Cost/Unit	Cost/Day
Tier 1	**FY 2005**	**7,043**	**33,752**	**1,548,474**	**1,416,343**	**$2,621,120.83**	**$1.69**	**$1.85**
(none)	FY 2004	5,769	26,207	1,232,361	1,108,883	$1,956,754.73	$1.59	$1.76
Tier 2	**FY 2005**	**442**	**2,132**	**110,382**	**103,672**	**$194,708.41**	**$1.76**	**$1.88**
(none)	FY 2004	508	2,212	115,473	106,565	$188,768.78	$1.63	$1.77

ACE Inhibitor/HCTZ Combinations

		Clients	Claims	Units	Days	Cost	Cost/Unit	Cost/Day
Tier 1	**FY 2005**	**3,408**	**16,079**	**841,992**	**708,133**	**$242,448.33**	**$0.29**	**$0.34**
	FY 2004	3,004	12,948	681,816	566,434	$329,897.42	$0.48	$0.58
Tier 2	**FY 2005**	**276**	**1,224**	**55,085**	**49,080**	**$62,019.58**	**$1.13**	**$1.26**
	FY 2004	195	793	41,547	34,938	$47,206.14	$1.14	$1.35

ACE Inhibitor/Calcium Channel Blocker Combinations

		Clients	Claims	Units	Days	Cost	Cost/Unit	Cost/Day
Tier 1	**FY 2005**	**2,397**	**11,457**	**560,403**	**495,331**	**$1,293,825.85**	**$2.31**	**$2.61**
	FY 2004	None	None	None	None	None	None	None
Tier 2	**FY 2005**	**16**	**92**	**6,149**	**4,774**	**$9,550.68**	**$1.55**	**$2.00**
	FY 2004	1,613	8,109	419,183	359,218	$897,472.56	$2.14	$2.50

ARB/HCTZ Combinations

		Clients	Claims	Units	Days	Cost	Cost/Unit	Cost/Day
Tier 1	**FY 2005**	**4468**	**21,107**	**1,060,482**	**941,233**	**$1,900,940.16**	**$1.79**	**$2.02**
(none)	FY 2004	3738	16,741	805,801	741,300	$1,419,952.29	$1.76	$1.92
Tier 2	**FY 2005**	**192**	**922**	**47,448**	**43,312**	**$97,640.10**	**$2.06**	**$2.25**
(none)	FY 2004	181	768	38,405	35,268	$73,798.70	$1.92	$2.09

ANTI-HYPERTENSIVE MEDICATIONS

CCB MEDICATIONS

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

ACE INHIBITORS

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

ACE/CCB COMBINATIONS

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

ACE/HCTZ COMBINATIONS

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

ARBs AND ARB/HCTZ COMBINATIONS

Tier 1	Tier 2
All ARBs and ARB/HCTZ combinations	

Products Moved to Tier-1

- felodipine (Plendil)
- quinapril (Accupril)
- diltiazem (Tiazac, Taztia XT)
- benazeparil/amlodipine (Lotrel)
- trandolapril/verapamil (Tarka)
- Atacand and Atacand/HCTZ (during FY 2006)

Trends in Utilization of Antihypertensives

When categorized by dual vs. non-dual eligible status, approximately 70% of the clients utilizing the class of antihypertensives are dual eligible clients. During fiscal year 2005 the dual eligible clients accounted for 75.6% of the claims and 77.6% of the costs.

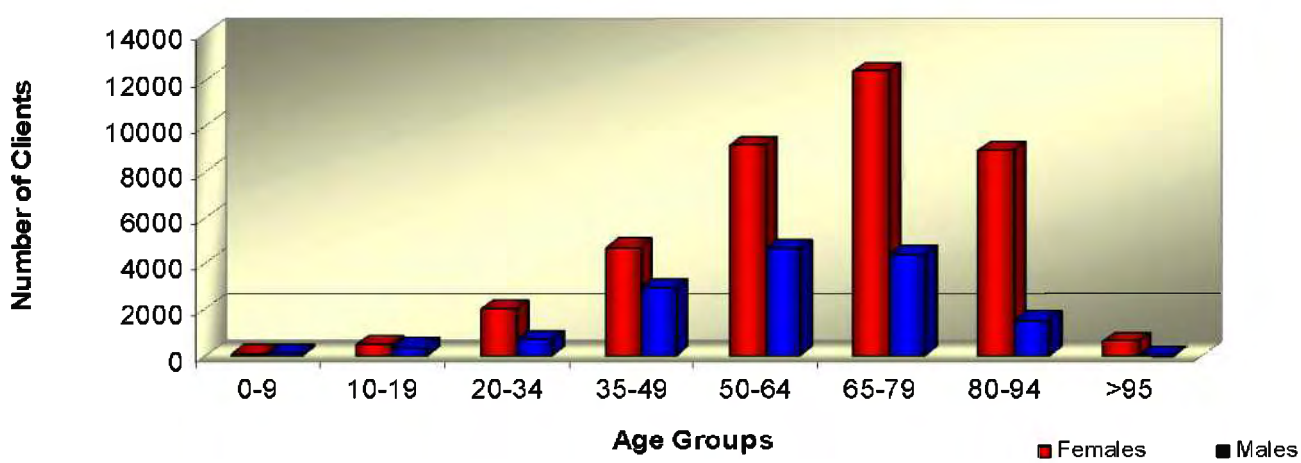
Utilization Comparison of Dual vs. Non-Dual Eligible Clients

	CLAIMS	UNITS	DAYS	CLIENTS	COST
Duals	260,296	12,733,475	10,582,216	37,127	$11,305,340.10
Non-Duals	83,775	4,237,112	3,456,278	16,259	$3,263,647.96
TOTALS	**344,071**	**16,970,588**	**14,038,494**	**53,386**	**$14,568,988.06**

Client Demographics

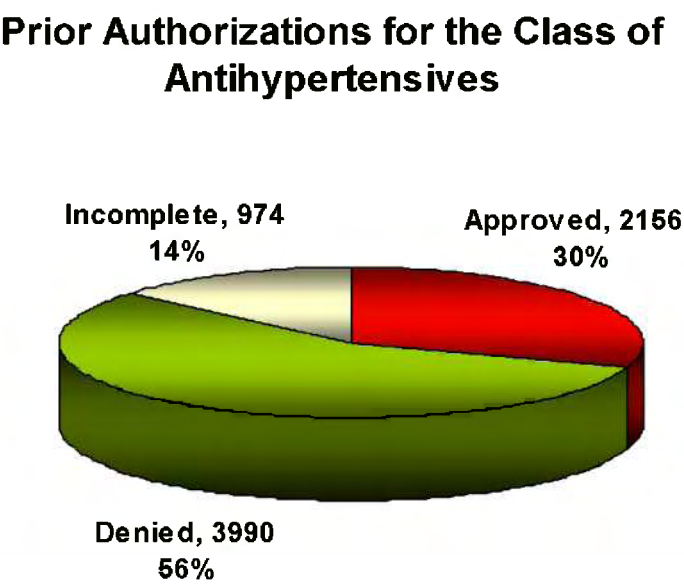
Age	Females	Dual	Non-Dual	Age	Males	Dual	Non-Dual
0-9	81	3	78	**0-9**	124	4	121
10-19	461	7	454	**10-19**	375	14	360
20-34	2,044	233	1,807	**20-34**	675	277	399
35-49	4,723	1,523	3,202	**35-49**	3,007	1,585	1,421
50-64	9,158	4,646	4,500	**50-64**	4,682	2,228	2,452
65-79	12,425	11,818	600	**65-79**	4,424	4,155	266
80-94	8,969	8,546	445	**80-94**	1,546	1,441	110
>95	629	589	38	**>95**	63	58	6
Totals	**38,490**	**27,365**	**11,124**	**Totals**	**14,896**	**9,762**	**5,135**

Demographics of All Clients Utilizing Antihypertensives



Prior Authorization of Antihypertensives

4,710 clients submitted a total of 7,120 prior authorization requests for an antihypertensive medication during fiscal year 2005. Of the 7,120 prior authorizations, 606 were for refill-too-soon overrides, and 210 were Pharmacotherapy Management petitions. The following are the statistics on prior authorizations submitted for this class. Please note 1,085 of the petitions that were initially denied or incomplete were later approved.



Amlodipine/Atorvastatin (Caduet)

Caduet® was voted by the DUR Board to be placed in the Product Based Prior Authorization program as a Tier-2 Calcium Channel Blocker in May of 2004 with the following criteria:

1. An FDA approved diagnosis from each drug category (CCB and HMG-CoA Reductase Inhibitor),
2. A documented failed trial of a Tier-1 CCB and
3. Concurrent use of an HMG-CoA Reductase Inhibitor.

Patients using both Norvasc® and Lipitor® were encouraged to switch to the appropriate strength of Caduet®. Caduet® was categorized as Tier-2 at the beginning of Fiscal Year 2005, but four months later, Caduet® was moved to Tier-1 due to manufacturer participation in the supplemental rebate program. The following is the utilization data for Caduet®.

	CLAIMS	UNITS	DAYS	CLIENTS	COST
Duals	683	31,358	31,011	244	$126,273.29
Non-Duals	290	14,965	14,385	125	$60,165.89
TOTALS	**973**	**46,323**	**45,396**	**369**	**$186,439.18**

70% of the clients were females and 66% were duals eligible clients. There were a total of five petitions submitted: one regular petition and four Pharmacotherapy Management petitions.

Recommendations

The College of Pharmacy has the following recommendation(s) for Fiscal Year 2006:

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

APPENDIX G

Prior Authorization Annual Review - Fiscal Year 2005

Smoking Cessation Products

Oklahoma Medicaid
February 2006

Prior Authorization

- All smoking cessation products are covered, including OTC products.
- All smoking cessation products are covered without prior authorization for the first 90 days.
- After 90 days of use in a 365 day period, further use of smoking cessation products requires prior authorization.
- Criterion for approval of PA after the first 90 days of use: petition must state that the patient is enrolled in a smoking cessation behavior modification program.
- Length of approval: PA can be approved for another 90 days.
- After the patient has had 180 days of treatment in a 365 day period, the patient must wait another 180 days before smoking cessation treatment will be covered again.
- Smoking cessation products do not count against the 6 prescription per month limit.

Utilization Fiscal Year 2005

For the period of July 2004 through June 2005, a total of **2,531** clients received smoking cessation products through the Medicaid fee-for-service program.

Product (unit)	# of Claims	Total Units	Total Days	Units/ Day	Total Cost	Total Clients	Per Diem
Zyban (ea)	461	26,977	14,381	1.88	$44,893.99	319	$3.12
Spray (ml)	91	5,860	1,353	4.33	$18,376.53	34	$13.58
Inhalers (cart)	737	120,364	15,965	7.54	$89,288.40	476	$5.59
Patches (ea)	3,341	78,692	77,810	1.01	$300,178.23	2,449	$3.94
Gum (ea)	57	8,359	1,147	7.29	$3,532.78	47	$3.08
Lozenges (ea)	100	16,160	1,768	9.14	$8,050.70	50	$4.55
Total FY '05	**4,787**	**256,412**	**112,424**	**2.28**	**$464,320.63**	**2,531***	**$4.13**

*Total unduplicated clients for FY05

Total Cost FY '05	**$464,320.63**
Total Cost FY '04	*$118,619.15*
Total Claims FY '05	**4,787**
Total Claims FY '04	*1,297*
Per Diem FY '05	**$4.13**
Per Diem FY '04	*$4.04*
Total Clients FY '05	**2,531**
*Total Clients FY '04**	732

Total petitions submitted in for this category during specified time period: 19

Approved 12
Denied 4
Incomplete 3

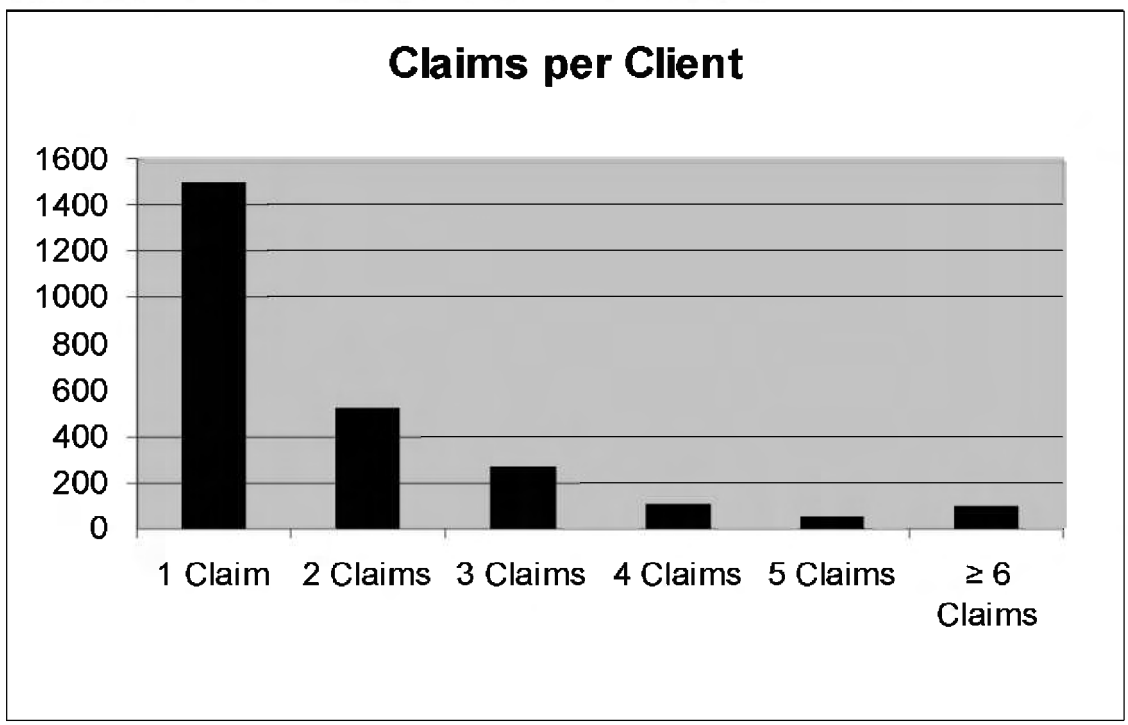
Demographics

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

Age	Female	Male	Totals
0 to 9	0	0	0
10 to 19	1	1	2
20 to 34	60	32	92
35 to 49	400	70	470
50 to 64	570	258	828
65 to 79	532	281	813
80 to 94	201	98	299
95 and Over	17	10	27
Totals	**1,781**	**750**	**2,531***

*Total unduplicated clients for FY'05

Claims reviewed to determine the number of claims per client.



Changes in Fiscal Year 2004

Effective February 1, 2004, all smoking cessation products were covered without prior authorization for the first 90 days. After 90 days of use in a 365 day period, further use of smoking cessation products required prior authorization.

Summer 2005, OHCA provider update newsletter featured an article on the free telephone-based Oklahoma Tobacco Helpline (1-866-PITCH-EM) funded by the Oklahoma Tobacco Settlement Endowment Trust.

Current News:

Biotechnology research by Zurich-based Cytos and British company Xenova are in early development stages of anti-smoking vaccines. These vaccines would encourage antibodies to bind to nicotine and reduce absorption in brain, therefore reducing the stimulant effect experienced by smokers.

December 2005 – FDA granted priority review of NDA for varenicline tartrate as a smoking cessation product. Partial nicotine agonist with selective nicotinic receptor modulator.

January 2006 – Patent expiration on Nicotrol® Inhaler

Recommendations

The College of Pharmacy recommends continued monitoring and evaluation of the cost and utilization of this PBPA category. In addition, recommend administering a tobacco cessation survey to clients whom have received previous smoking cessation products to evaluate effectiveness of treatment and participation in smoking cessation programs.

APPENDIX H

Annual Review of Growth Hormones - Fiscal Year 2005

Oklahoma Medicaid
February 2006

Definition of Prior Authorization Category for FY '05

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

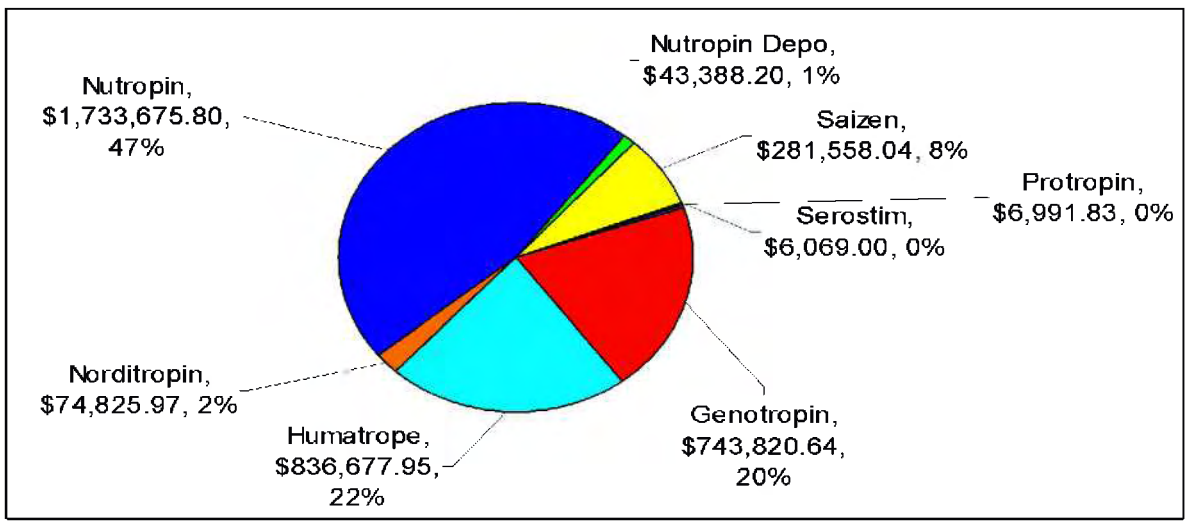
For the period of July 2004 through June 2005, a total of 215 clients received growth hormone products through the Medicaid fee-for-service program. One of these clients is a dual-eligible. (Total cost for dual eligible client is $17,101.17, includes dispensing fees)

Product	# of Claims	Total Units	Total Days	Units /Day	Total Cost	Total Clients	Cost/mg**
Protropin 10 mg	3	15	99	0.15	$6,991.83	1	$47.61
Nutropin AQ 5mg/ml	550	4,314	15,094	0.28	$1,002,150.94	111	$46.46
Norditropin 5mg/1.5ml	22	124	709	0.17	$20,424.56	7	$32.94
Norditropin 15mg/1.5ml	37	128	1,089	0.12	$54,401.41	8	$28.33
Humatrope 5 mg	82	691	2,452	0.28	$161, 916.67	12	$46.86
Nutropin 5 mg	40	249	1,167	0.50	$52,381.19	4	$42.07
Genotropin 5.8 mg	129	666	3,730	0.21	$157,482.46	15	$40.77
Humatrope 6 mg	102	258	2,740	0.09	$76,953.22	16	$49.74
Humatrope 12 mg	117	326	3,448	0.09	$183,994.83	15	$47.03
Genotropin 13.8 mg	113	569	2,900	0.2	$295,429.25	15	$37.62
Nutropin 10 mg	220	1,372	5,918	0.23	$679,143.67	22	$49.50
Humatrope 24 mg	77	359	2,372	0.15	$413,813.23	11	$48.03
Genotropin 0.2 mg	27	742	758	1.00	$7,142.86	3	$48.13
Genotropin 0.4 mg	3	84	84	1.00	$1,506.50	2	$44.84
Genotropin 0.6 mg	41	1,192	1,187	1.00	$34,003.15	6	$47.54
Genotropin 0.8 mg	27	756	756	1.00	$27,695.49	4	$45.79
Genotropin 1 mg	33	941	954	1.00	$44,701.24	5	$47.50
Genotropin 1.2 mg	1	28	28	1.00	$1,633.95	1	$48.63
Genotropin 1.4 mg	9	252	252	1.00	$13,239.14	2	$37.53
Genotropin 1.6 mg	25	717	711	1.00	$53,928.51	4	$47.01
Genotropin 1.8 mg	17	476	478	1.00	$40,466.80	3	$47.23
Genotropin 2 mg	25	700	700	1.00	$66,591.29	3	$47.56
Nutropin Depot 13. mg	10	28	254	0.11	$17,011.72	1	$44.39
Nutropin Depot 18mg	13	26	390	0.06	$26,376.48	2	$43.64
Saizen 5 mg	25	276	667	0.41	$62,888.26	3	$45.57
Serostim 6 mg	1	28	28	1.00	$6,069.00	1	$36.13
Saizen 8.8 mg	61	617	1,801	0.34	$218,669.78	86	$40.27
Total	**1,810**	**15,933**	**50,765**	**0.43**	**$3,727,007.73**	**215***	**$44.03*****

*Total unduplicated clients for FY05.
**Cost calculations include dispensing fee, but not rebate information.
*** Average of cost/mg.

Total Cost FY '05	**$3,727,007.43**
Total Cost FY '04	*$2,256,166.18*
Total Claims FY '05	**1,810**
Total Claims FY '04	*1,074*
Total Clients FY '05	**215**
Total Clients FY '04	*168*

Market Share



PA Activity

Total petitions submitted in for this category during specified time period: 494

Approved	436
Denied	30
Incomplete	28

Demographics

Age	Female	Male	Totals
0 to 9	37	46	83
10 to 19	36	78	114
20 to 34	4	6	10
35 to 49	4	3	7
50 to 64	0	0	0
65 to 79	1	0	1
80 to 94	0	0	0
95 and Over	0	0	0
Totals	82	133	215

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

Changes in FY '05

- Nutropin depot (Genentech) was taken off the market in June 2004. All clients using the depot product have been changed to a daily injection.
- Zorbtive™ (Serono) [somatropin (rDNA origin, mammalian derived) for injection] for use in the treatment of patients with short bowel syndrome was introduced in May, 2004. There has been no use of this product.
- A new product, TEV-TROPIN® (GATE Pharmaceuticals), introduced to the market in January, 2005 for classic hGH deficiency, has had no usage in the Oklahoma Medicaid population.

New in FY '06

Increlex™ (mecasermin) (Tercica) and iPlex™ (mecasermin rinfabate) (Insmed, Inc), have been approved in the last several months for severe primary insulin-like growth factor-1 (IGF-1) deficiency. Increlex™ does not currently have a rebate agreement with CMS. iPlex™ is not yet available on the market.

Recommendations

The College of Pharmacy has the following recommendation(s) for Fiscal Year 2004:

- Change criterion for initiation of therapy of growth hormone from bone age delay of two years or more to bone age delay >2 standard deviations below the mean for age[1].
- The College of Pharmacy recommends the addition of the IGF-1 replacement therapy to the Prior Authorization program if the manufacturers sign federal drug rebate agreements.

1. Wilson T, Rose S, Cohen P, et al. Update of Guidelines for the use of Growth Hormone in Children: The Lawson Wilkins Pediatric Endocrinology Society Drug and Therapeutics Committee. J Pediatr 2003:143:415-21.

APPENDIX I

Fuzeon®(enfuvirtide) Follow Up Review

Oklahoma Medicaid
February 2006

Fuzeon® Convenience Kit (60 single-use vials, with sterile water, syringes, & alcohol wipes = 30 days of medication per kit). AWP = $ 2,315.40

Fuzeon® is a fusion inhibitor manufactured by Trimeris and Roche to be used in combination with other antiretroviral agents as indicated for the treatment of HIV-1 infection. It was approved in March, 2003 by the FDA. It was approved for HIV-positive people who have tried other anti-HIV drugs in the past and are unable to keep their viral loads undetectable using drugs that were currently available. It has not yet been approved for use without other anti-HIV drugs or for treatment naïve HIV-positive people. It works best when combined with at least two other anti-HIV drugs that the patient's virus has shown to be sensitive.

Fuzeon® works by binding to a protein called gp41 on HIV's surface. Once the protein is bound, HIV cannot successfully bind with the surface of T-cells, this prevents the virus from infecting healthy cells. Currently it is administered twice a day. However, the manufacturers are experimenting with needle-free injection equipment changing it to once a day dosing. If these improvements prove to be safe and effective, it may be approved by the FDA this year.

FY 04/05 Utilization Comparison

Total Cost FY '05	**$184,421.99**
Total Cost FY '04	*$97,359.64*
Total Claims FY '05	**75**
Total Claims FY '04	*53*
Total Clients FY '05	**14**
Total Clients FY '04	*10*
Per Diem FY '05	**$76.14**
Per Diem FY '04	*$61.69*

Market Changes:
Roche and Trimeris are currently working on two next-generation fusion inhibitor peptides which have been derived from HR2 sequences of HIV. Their goal is to reach longer suppression of HIV by increasing the genetic barrier to resistance development and having higher potency molecules. With these new molecules they are working toward a once-weekly dose.

Recommendations:
Continue monitoring use annually. There does not appear to be any inappropriate use of this medication at this time.

References:

1. AidsMeds. Fuzeon® (enfuvirtide, T-20). From http://www.aidsmeds.com/drugs/Fuzeon.htm

2. Sandoz: Roche and Trimeris Announce Selection of Two Next Generation HIV Fusion Inhibitor Drug Candidates for Development.
   From http://sandoz.yellowbrix.com/pages/sandoz/Story.nsp?story_id=88109771

APPENDIX J

30 Day Notice of Intent to Prior Authorize Ultram® ER (tramadol HCl) Extended-Release Tablets and Ultram® ODT (tramadol HCl) Orally Disintegrating Tablets

Oklahoma Medicaid
February 2006

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

Summary

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

Ultram® ODT is an orally disintegrating formulation of tramadol. It is indicated for the treatment of moderate to moderately severe pain in adults and will be available in a 50 mg dosage form. It is expected to be launched in the second quarter of 2006.

Recommendations

The College of Pharmacy recommends Prior Authorization of Ultram® ER and ODT. Criteria for approval of the ER formulation would include an FDA approved diagnosis for the use of Ultram® ER, a diagnosis indicating that the client has a condition that requires extended pain treatment with an around-the-clock dosing schedule, the reason immediate release tramadol is inappropriate, and the physician's signature.

Criteria for approval of the ODT formulation would include an FDA approved diagnosis for the use of Ultram® ODT, a diagnosis indicating that the client has a condition that prevents them from swallowing tablets, and the physician's signature.

The College of Pharmacy also recommends quantity limits of 30 units for 30 days for the ER and 240 units for 30 days for the ODT (unless another FDA dosage is approved). Currently Ultram® has a quantity limit of 240 units for 30 days.

Cost comparison

	Estimated Acquisition Cost (EAC) / Unit	Daily Dose	Monthly Dose (30 day supply)	Cost for 30 day supply
Tramadol 50 mg tablets	$ 0.05488*	Up to 400 mg	240 tablets	$ 13.17
Ultram® 50 mg tablets	$ 1.16670	Up to 400 mg	240 tablets	$ 280.01†
Ultram® ER 100mg tablets	$ 2.86000	Up to 300mg	30 tablets	$ 85.80
Ultram® ER 200mg tablets	$ 4.73000	Up to 200mg	30 tablets	$ 141.90
Ultram® ER 300mg tablets	$ 6.60000	Up to 300mg	30 tablets	$ 198.00
Ultram® ODT	Unavailable	Unavailable	Unavailable	Unavailable

*SMAC Pricing
†DAW Rule Applies

Reference

1. Ultram® ER Prescribing Information. PriCara, Unit of Ortho-McNeil, Inc. 2005.
2. Biovail, Ortho-McNeil Partnership Receives Hart-Scott-Rodino Regulatory Clearance. December 2, 2005. Available at: http://www.biovail.com/english/Investor%20Relations/Latest%20News/default.asp?s=1&state=showrelease&releaseid=792341. Accessed January 28, 2006.

New Product Summaries

Oklahoma Medicaid
February 2006

Drug	Manufacturer	Indications	Dosage	Adverse Effects	Contraindications	New Molecular Entity	AWP/ unit
Exubera® (insulin human [rDNA origin]) Inhalation Powder	Pfizer Inc.	Treatment of adult patients with diabetes mellitus for the control of hyperglycemia.	Initial dosing is individualized and determined based on needs of the patient. Initial pre-meal dosing formula: Body wt (kg) X 0.05 mg/kg = pre-meal dose (mg) (rounded down to nearest whole number). Should be given with in 10 minutes of a meal.	Non-Resiratory: hypoglycemia, chest pain, dry mouth, otitis media; Respiratory: infection, cough, pharyngitis, rhinitis, sinusitis, respiratory disorder, dypsnea, sputum increased bronchitis, asthma, epistaxis, laryngitis, pneumonia, voice alteration.	Hypersensitivity to Exubera® or one of its excipients, patients who smoke or who have discontinued smoking less than 6 months prior to starting therapy (DC is smoking starts or resumes), patients with unstable or poorly controlled lung disease.	No	N/A
Orencia® (abatacept) lyophilized powder for IV infusion	Bristol-Myers Squibb Company	Reducing signs and symptoms, inducing major clinical response, slowing the progression of structural damage, and improving physical function in adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response to one or more DMARDs.	Administered as a 30-minute intravenous infusion. After initial infusion it should be given at 2 and 4 weeks then every 4 weeks thereafter. Dosing is weight based with the maximum dose of 1 gram per infusion.	Infections and malignancies were the major adverse reactions, acute infusion-related reactions, hypersensitivity, headache, nasopharyngitis, dizziness, cough, back pain, hypertension, dyspepsia, UTI, rash, and pain in extremity.	Hypersensitivity to Orencia® or any of its components.	Yes	$562.50 / 250 mg vial

APPENDIX K

FDA News

FOR IMMEDIATE RELEASE
P06-13
January 27, 2006

Media Inquiries:
Laura Alvey, 301-827-6242
Consumer Inquiries:
888-INFO-FDA

FDA Approves First Ever Inhaled Insulin Combination Product for Treatment of Diabetes

There is a new, potential alternative for many of the more than 5 million Americans who take insulin injections, with the Food and Drug Administration's approval today of the first ever inhaled insulin. Exubera, an inhaled powder form of recombinant human insulin (rDNA) for the treatment of adult patients with type 1 and type 2 diabetes, is the first new insulin delivery option introduced since the discovery of insulin in the 1920s.

"Until today, patients with diabetes who need insulin to manage their disease had only one way to treat their condition," said Dr. Steven Galson, Director, Center for Drug Evaluation and Research, FDA. "It is our hope that the availability of inhaled insulin will offer patients more options to better control their blood sugars."

Diabetes is a disease that affects the amount of insulin and sugar in your body. Exubera is a human form of insulin and as such, lowers blood sugar concentrations by allowing the blood sugar to be taken up by cells as a source of fuel. Exubera is a powdered form of insulin that is able to be inhaled into the lungs through the patient's mouth using a specially designed inhaler.

There are two major types of diabetes — type 1 and type 2. People with type 1 diabetes produce virtually no insulin. In type 2, the most common form of the disease, the body does not produce enough insulin or effectively use insulin. If people with diabetes do not properly control their blood sugar levels, serious complications including heart disease, kidney failure, blindness, and nerve damage may develop.

The safety and efficacy of Exubera have been studied in approximately 2500 adult patients with type 1 and type 2 diabetes. In clinical studies, Exubera reached peak insulin concentration more quickly than some insulins, called regular insulin, administered by an injection. Peak insulin levels were achieved at 49 minutes (range 30 to 90 minutes) with Exubera inhaled insulin compared to 105 minutes (range 60 to 240 minutes) with regular insulin, respectively. In type 1 diabetes, inhaled insulin may be added to longer acting insulins as a replacement for short-acting insulin taken with meals. In type 2 diabetes, inhaled insulin may be used alone, along with oral (non-insulin) pills that control blood sugar, or with longer acting insulins.

Exubera prescriptions will be accompanied by a Medication Guide containing FDA-approved information written especially for patients. Pharmacists are required to distribute Medication Guides with products FDA has determined are important to health, and patient adherence to directions for use is crucial to the product's effectiveness. Patients are advised to read the entire Medication Guide and talk to their healthcare provider if they have further questions.

Like any insulin product, low blood sugar is a side effect of Exubera and patients should carefully monitor their blood sugars regularly. Other side effects associated with Exubera therapy seen in clinical trials included cough, shortness of breath, sore throat, and dry mouth.

Exubera is not to be used if you smoke or if you recently quit smoking (within the last 6 months). Exubera is not recommended in patients with asthma, bronchitis, or emphysema. Baseline tests for lung

function are recommended before beginning treatment and are recommended to be repeated every 6 to 12 months thereafter.

While Exubera has been extensively studied for safety, the sponsor has committed to performing long-term studies to confirm the continued safety of Exubera after it is marketed and to examine more thoroughly the issue of the efficacy and safety of Exubera in patients with underlying lung disease.

Exubera is manufactured by Pfizer Inc., NY, NY.

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FDA News

FOR IMMEDIATE RELEASE
P06-09
January 19, 2006

Media Inquiries:
Susan Cruzan, 301-827-6242
Consumer Inquiries:
888-INFO-FDA

FDA Approves Updated Labeling with Boxed Warning and Medication Guide for Two Eczema Drugs, Elidel and Protopic

The Food and Drug Administration (FDA) today announced the approval of updated labeling for two topical eczema drugs, Elidel Cream (pimecrolimus) and Protopic Ointment (tacrolimus). The labeling will be updated with a boxed warning about a possible risk of cancer and a Medication Guide (FDA-approved patient labeling) will be distributed to help ensure that patients using these prescription medicines are aware of this concern. The new labeling also clarifies that these drugs are recommended for use as second-line treatments. This means that other prescription topical medicines should be tried first. Use of these drugs in children under 2 years of age is not recommended.

Eczema or atopic dermatitis is one of the most common skin disorders seen in infants and children, affecting 10 to 15 percent of the childhood population. Although the cause of atopic dermatitis is not known, it is thought that there may be an allergic or immune mediated component. Patients have chronic itching and dry skin, which results in redness and damage to the skin due to rubbing and scratching. Both products are applied to the skin to help control eczema. It is not known exactly how the products work, but they have various effects on the body's immune system.

"We are taking steps to ensure that healthcare providers and patients are aware of the possible long-term risks of these products so that they will be used appropriately", said Dr. Steven Galson, Director of FDA's Center for Drug Evaluation and Research (CDER). "Today's actions are aimed at making sure that health care providers and consumers understand the new warnings and that it is important that these products be used as recommended in the label."

On February 15, 2005, FDA's Pediatric Advisory Committee recommended that the labeling should be updated with a boxed warning and a Medication Guide about the possible cancer risk for these drugs. FDA had issued a Public Health Advisory in March 2005 advising physicians about the possible cancer risk. At the same time, FDA indicated it would ask the sponsors to update the labeling to address this possible risk. Although a causal link has not been established, rare reports of cancer (for example, skin and lymphoma) have been reported in patients who had been receiving these products.

The boxed warning informs healthcare professionals that the long term safety of these drugs has not been established. Although studies are being conducted by the manufacturers of both drugs to try to answer questions about cancer risk, it could be many years before the research is concluded. In the meantime, there is a benefit associated with these drugs when used appropriately. For instance, they may be effective when other prescription topical medications do not work or are not advisable for the patient. The drugs are intended to be used for short periods, but if a patient requires a longer period of treatment, the treatment can be repeated after a period of time off treatment. Patients are advised to call their doctor if symptoms worsen, they develop an infection, or if symptoms do not improve within the six weeks of treatment.

The Medication Guide will provide consumer friendly information to patients about how to use the drugs safely. Pharmacists are required to provide the Medication Guide to patients when dispensing the drug. Patients are advised to read the entire Medication Guide and talk to their healthcare provider if they have further questions.

Novartis manufactures Elidel cream and Astellas Pharma, Inc (formerly Fujisawa Healthcare) is the manufacturer of Protopic ointment.

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Elidel Information

- Label
- Medication Guide

Protopic Information

- Label
- Medication Guide

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FDA Public Health Advisory
Ketek (telithromycin) Tablets

Today, January 20, 2006, *Annals of Internal Medicine* published an article reporting three patients who experienced serious liver toxicity following administration of Ketek (telithromycin). These cases have also been reported to FDA MedWatch. Telithromycin is marketed and used extensively in many other countries, including countries in Europe and Japan. While it is difficult to determine the actual frequency of adverse events from voluntary reporting systems such as the MedWatch program, the FDA is continuing to evaluate the issue of liver problems in association with use of telithromycin in order to determine if labeling changes or other actions are warranted. As a part of this, FDA is continuing to work to understand better the frequency of liver-related adverse events reported for approved antibiotics, including telithromycin.

While FDA is continuing its investigation of this issue, we are providing the following recommendations to healthcare providers and patients:

- Healthcare providers should monitor patients taking telithromycin for signs or symptoms of liver problems. Telithromycin should be stopped in patients who develop signs or symptoms of liver problems.
- Patients who have been prescribed telithromycin and are not experiencing side effects such as jaundice should continue taking their medicine as prescribed unless otherwise directed by their healthcare provider.
- Patients who notice any yellowing of their eyes or skin or other problems like blurry vision should contact their healthcare provider immediately.
- As with all antibiotics, telithromycin should only be used for infections caused by a susceptible microorganism. Telithromycin is not effective in treating viral infections, so a patient with a viral infection should not receive telithromycin since they would be exposed to the risk of side effects without any benefit.

The case review in today's online publication by *Annals of Internal Medicine* reports three serious adverse events following administration of telithromycin. All three patients developed jaundice and abnormal liver function. One patient recovered, one required a transplant, and one died. When the livers of the latter two patients were examined in the laboratory, they showed massive tissue death. These two patients had reported some alcohol use. All three patients had previously been healthy and were not using other prescription drugs. The FDA is also aware that these patients were all treated by physicians in the same geographic area. The significance of this observation is not clear at the present time.

In pre-marketing clinical studies, including a large safety trial and data from other countries, the occurrence of liver problems was infrequent and usually reversible. Based on the pre-marketing clinical data, it appeared that the risk of liver injury with telithromycin was similar to that of other marketed antibiotics. Nonetheless, the product label advises doctors about the potential for liver-related adverse

events associated with the use of telithromycin.

Telithromycin is an antibiotic of the ketolide class. It was the first antibiotic of this class to be approved by the FDA in April, 2004 for the treatment of respiratory infections in adults caused by several types of susceptible microorganisms including *Streptococcus pneumoniae* and *Haemophilus influenzae*.

Back to Top Back to Ketek

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FDA News

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Media Inquiries:
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Consumer Inquiries:
888-INFO-FDA

FDA Announces New Prescription Drug Information Format to Improve Patient Safety

The U.S. Food and Drug Administration (FDA) today unveiled a major revision to the format of prescription drug information, commonly called the package insert, to give healthcare professionals clear and concise prescribing information. In an effort to manage the risks of medication use and reduce medical errors, the newly designed package insert will provide the most up-to-date information in an easy-to-read format that draws physician and patient attention to the most important pieces of drug information before a product is prescribed. The new format will also make prescription information more accessible for use with electronic prescribing tools and other electronic information resources.

"Providing healthcare professionals and patients with clear and concise information about prescriptions will help ensure safe and optimal use of drugs, which translates into better health outcomes for patients and more efficient delivery of healthcare," said HHS Secretary Mike Leavitt. "By improving the package insert to make it more useful for healthcare providers in their day-to-day clinical practice, we are making it easier for them to explain the benefits and risks of medications for their patients."

Each year, approximately 300,000 preventable adverse events occur in hospitals in this country, many as a result of confusing medical information. Research shows that prioritizing the warning information has a greater impact on reducing such events. Therefore, the new prescription label format provides the most important information about a prescription product in a format that is better understood, more easily accessible and more memorable for physicians. By making these changes, FDA is seeking to reduce the complexity of information on prescription drug labels, making them more useful for physicians and their patients.

"Americans are overwhelmed with the complexity of health information. We have hit a point of information overload and the public health message is being diluted," said Richard H. Carmona, M.D., M.P.H., FACS, U.S. Surgeon General. "This is of great concern when it comes to making sure a patient knows how to use prescription drugs safely and effectively. This problem is compounded by prescription medication information that reads more like legal disclaimers than useful or actionable health information."

Revised for the first time in more than 25 years, the new format requires that the prescription information for new and recently approved products meet specific graphical requirements and includes the reorganization of critical information so physicians can find the information they need quickly. Some of the most significant changes include:

- A new section called *Highlights* to provide immediate access to the most important prescribing information about benefits and risks.
- A *Table of Contents* for easy reference to detailed safety and efficacy information.
- The date of initial product approval, making it easier to determine how long a product has been on the market.
- A toll-free number and Internet reporting information for suspected adverse events to encourage more widespread reporting of suspected side effects.

"The new label design makes it easier for doctors to get access to important information about drug safety and benefits, and this in turn will help them have more meaningful discussions with their patients," said Andrew von Eschenbach, M.D., FDA Acting Commissioner of Food and Drugs. "This redesigned label is a big step in our commitment to giving health professionals the tools and information they need to optimize their clinical practice and choose among a growing number of effective treatments to make more personalized prescribing decisions for their patients."

The most notable change is the addition of a summary outlining the most important information about a product, prominently displayed at the top of the page. Designed to help healthcare professionals find the information they need quickly, *Highlights* will typically be half a page in length and will provide a concise summary of information about specific areas including: *Boxed Warning, Indications and Usage,* and *Dosage and Administration;* and will refer the healthcare professional to the appropriate section of the *Full Prescribing Information*. In addition, drug makers will be required to include a list of all substantive recent changes made within the year, to ensure healthcare professionals have immediate access to the most up-to-date information about the product before prescribing it.

Over the past ten years, the prescribing information for newly approved products has become increasingly more complex, and specific information is often difficult to locate. Physicians will now be able to find critical information more quickly, through a new *Table of Contents* that refers readers to detailed information located in the label. The *Full Prescribing Information* is reorganized to give greater prominence to the most important and most commonly referenced information. As a result of feedback from two national physician surveys, the *Indications and Usage* and the *Dosage and Administration* sections are moved to the beginning of *the Full Prescribing Information.*

The addition of a new *Patient Counseling Information* section places greater emphasis on the importance of communication between professionals and patients. This new section is designed to help doctors advise their patients about important uses and limitations of medications. It will also serve as a guide for discussions about the potential risks involved in taking a specific treatment and steps for managing those risks. If FDA has approved patient information for a prescription drug, it will be printed at the end of the label immediately following the *Patient Counseling Information* section or will accompany the label so it can be easily shared.

"In the last month, we have announced important steps toward creating an electronic environment for drug safety and effectiveness information that can provide patients and healthcare professionals with critical information at the point of care," said von Eschenbach. "This revised prescription information format, in combination with new requirements for electronic labels announced earlier this month and requirements for barcodes on drugs will dramatically improve the way healthcare professionals and consumers obtain information about prescription drugs."

The new prescription information format will be integrated into FDA's other e-Health initiatives and standards-setting efforts through a variety of ongoing initiatives at the agency. As prescription information is updated in this new format it will be used to provide medication information for *DailyMed* -- a new interagency online health information clearinghouse that will provide the most up-to-date medication information free to consumers, healthcare professionals and healthcare information providers. The *DailyMed* is now making up-to-date information about FDA-regulated products widely available on the Internet free of charge. This information can be accessed through the National Library of Medicine at http://dailymed.nlm.nih.gov. In the future, this new information will also be provided through a website called facts@fda, a comprehensive Internet resource designed to give one-stop access for information about all FDA-regulated products.

In December 2000, before issuing the proposed rule the agency evaluated extensive information it received on the usefulness of the present prescription drug labeling for healthcare professionals to determine how content and format could be improved. The agency used feedback from focus groups, national physician surveys, a public meeting and written comments to design the new prescription information format. FDA determined the most common practices for using prescription drug labeling, as well as information considered to be most important, and then developed the new format based on this information. The new drug labeling requirements will be phased in gradually and initially will apply to newly and recently approved prescription drugs and drugs that receive approval for new uses. The agency is encouraging drug makers to consider complying with the new labeling requirements earlier on a voluntary basis. All drugs approved within the past five years are included, and they will gradually be converted to the new prescribing information format.

For additional information, please visit CDER's website:
http://www.fda.gov/cder/regulatory/physLabel/default.htm

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Final Guidances for Industry: Content and Format of Labeling for Human Prescription Drug and Biological Products
Federal Register [PDF, 520KB]
Guidance: Clinical Studies [PDF, 127KB]
Guidance: Adverse Reactions [PDF, 52KB]

Draft Guidances for Industry: Content and Format of Labeling for Human Prescription Drug and Biological Products
Federal Register [PDF, 483KB]
Draft Guidance: Implementing the New Content and Format Requirements [PDF, 214KB]
Draft Guidance: Warnings and Precautions, Contraindications, and Boxed Warning [PDF, 58KB]

Final Rule: Requirements on Content and Format of Labeling for Human Prescription Drug and Biological Products
Final Rule: Part 1 [PDF, 9.7MB]
Final Rule: Part 2 [PDF, 9.9MB]
Final Rule: Part 3 [PDF, 6.7MB]

Better Prescription Drug Information (Slides from Jan. 18 Press Conference)

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