Drug Utilization Review Board

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

May 10, 2005 @ 6:00 p.m.

THE UNIVERSITY OF OKLAHOMA

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MEMORANDUM

TO: Drug Utilization Review Board Members

FROM: Ron Graham, D.Ph.

SUBJECT: **Packet Contents for Board Meeting – May 10, 2005**

DATE: May 4, 2005

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

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

Call to Order

Public Comment Forum

New Legislature Update and Budget Issues

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

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

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

30 Day Notice of Intent to Prior Authorize Zelnorm® – **See Appendix D.**

30 Day Notice of Intent to Prior Authorize Niravam® – **See Appendix E.**

30 Day Notice of Intent to Prior Authorize Symlin® – **See Appendix F.**

Review and Discuss Antihyperlipidemic Utilization – **See Appendix G.**

Review and Discuss Elidel® and Protopic® – **See Appendix H.**

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

Future Business

Adjournment

Drug Utilization Review Board

(DUR Board)

Meeting – May 10, 2005 @ 6:00p.m.

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

AGENDA

Discussion and Action On the following Items:

Items to be presented by Dr. Whitsett, Chairman:

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

Items to be presented by Dr. Whitsett, Chairman:

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

Items to be presented by Nico Gomez, Dr. Whitsett, Chairman:

3. Legislature Update and Budget Issues

Items to be presented by Dr. Whitsett, Chairman:

4. Action Item - Approval of DUR Board Meeting Minutes – See Appendix A.
- A. April 12, 2005 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 Report for February 2005
- B. Medication Coverage Activity Audit for April 2005
- C. Help Desk Activity Audit for April 2005

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

6. Action Item – Vote to Prior Authorize Antidepressants – See Appendix C.
- A. Recommended Prior Authorization Criteria
- B. Recommended Tier List

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

7. 30 Day Notice of Intent to Prior Authorize Zelnorm® – See Appendix D.
- A. COP Recommendations
- B. Potential Economic Impact

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

8. 30 Day Notice of Intent to Prior Authorize Niravam® – See Appendix E.
- A. COP Recommendations
- B. New Product Information

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

9. 30 Day Notice of Intent to Prior Authorize Symlin® – See Appendix F.
- A. COP Recommendations
- B. New Product Information

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

10. Review and Discuss Antihyperlipidemic Utilization – See Appendix G.
- A. Disease State
- B. Product Review
- C. Utilization Review
- D. COP Recommendations

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

11. Review and Discuss Elidel® and Protopic® – See Appendix H.
- A. Product Review
- B. Utilization Review
- C. COP Recommendations

12. FDA and DEA Updates – See Appendix I.

13. Future Business
- A. Antifungal Review
- B. Estrogen Replacement Products Review
- C. Neurontin™ Follow-Up Review
- D. Renal Product Review
- E. Utilization Review Comparisons for Previous Fiscal Years
- G. New Product Reviews

14. Adjournment

APPENDIX A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of APRIL 12, 2005

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

COLLEGE of PHARMACY STAFF:	PRESENT	ABSENT
Leslie Browning, D.Ph., 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 Kim Le, Pharm.D., Clinical Pharmacist	X	
Ann McIlvain, Pharm.D., Clinical Coordinator	X	
Carol Moore, Pharm.D., Clinical Pharmacist		X
Neeraj Patel, Pharm.D., Clinical Pharmacist		X
Lester A. Reinke, Ph.D., Associate Dean		X
Visiting Pharmacy Student: Nonye Okeke	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
Lynn Mitchell, M.D., M.P.H., Director of Medicaid/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	

OTHERS PRESENT:

Alan Barreuther, Purdue Pharma LP	Kristi L. Robinson	Courtney L. Walker, Lilly
Evie Knisely, Novartis/Genentech	Joe Rippager, MD	Rhonda Clark, Purdue
Toby Thompson, Pfizer	Mark DeClerk, Lilly	Sheila Thomas, Lilly
Charlene Kaiser, Wyeth	Greg Hoke, Wyeth	Richard Ponder, J&J
Ron Schnare, Abbott	Meg Draper, Lilly	(Illegible) Ruble, Ruble Associates
Pat Evans, BMS	Debbie Bower, Novartis	Julie Kamp, LPN
Jason Schwier, Amgen	Robb Host, Cephalon	Mike Avey, Sepracor
Jim Dunlap, Lilly	Jeff Knappen, Allergan	Andi Moore, Takeda
Dale Roof, Takeda	Donna Erwin, BMS	Jorge Nassar, BMS
Ritchie Sontz, Alpharm		

PRESENT FOR PUBLIC COMMENT:

Joe Rippager, MD	Agenda Item No. 6
Courtney L. Walker, Lilly	Agenda Item No. 6
Evie Knisely, Novartis/Genentech	Agenda Item No. 8, 10
Kristi L. Robinson	Agenda Item No. 8
Alan Barreuther, Purdue Pharma LP	Agenda Item No. 9

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 speakers for Public Comment.

ACTION: NONE REQUIRED.

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

3A: March 8, 2005 DUR Minutes

Dr. Meece moved to approve minutes; second by Dr. McNeill.

ACTION: MOTION CARRIED.

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

4A: Retrospective Drug Utilization Review Report for December 2004, January 2005

4B: Medication Coverage Activity Report: March 2005

4C: Help Desk Activity Report: March 2005

4D: Pharmacotherapy Management Program – Quarterly Report

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

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 5: **ANNUAL REVIEW OF SMOKING CESSATION PRODUCTS**

For Public Comment: Tracy Strader, Director of Tobacco Settlement Endowment Trust (presenting for Linda Wright Eakers):

I understand you all are going to be looking at the utilization of the pharmacotherapy benefit for tobacco independence treatment and a piece of that, I hope, is coupled with the Oklahoma Tobacco Helpline. Have most of you heard of the helpline? Okay. So Linda's sick today and extends her apologies in a very hoarse voice. I have a few handouts – probably not enough for the whole group here, but it's just of the presentation. I will say Linda can be contacted or you can contact me at our office if you want any of the materials in terms of referring patients or just the little business cards and that kind of thing. And I apologize. This was a draft that I had, but we do have now a Spanish-speaking number that's not just a bunch of X's, so it's a direct line that people who speak Spanish can call and actually have the phone answered in Spanish, so I'll get that to you all later. I just didn't happen to have that at my fingertips when I looked at this, but the main number is 1-866-PITCH-EM or (1-866)748-2436. We're going into "what is a helpline" first, I guess. Basically are most of you familiar with helpline services in general or how they fit in the context of an overall program? They really serve as sort of a basic piece of infrastructure from which I think all sorts of cessation programs can have an interplay. So if you've got community based services available, the helpline can serve as information and referral, but certainly the main function of the helpline is to provide the counseling services either in a one call format, depending on what the client identifies as being ready or willing to engage in, or up to five calls. Each of these are with a tobacco treatment specialist and the specialist makes all of the calls proactively to the person, to the participant. The very first call may be made by the participant to enroll in services or what I call register for services, but also they can be referred through a fax referral form, and from that the helpline service can actually just make the initial call a proactive call. And the research is pretty clear that it's those proactive calls, it's reaching out to them and offering the service that's actually the very most effective strategy. They utilize the stage of change or transtheoretical model to help identify where people are in their quitting process, if they're just thinking about it, or getting ready, or actively engaging in quitting, or if they need some relapse prevention assistance. They use a cognitive behavioral approach and motivational interviewing is a cornerstone for most tobacco help lines in that they really try to roll with the resistance and help people move along at their own pace. Sometimes we call it coaching. That seems to be a little bit more palatable than counseling for some. Whatever will work. Right now the helpline is funded entirely by the Oklahoma Tobacco Settlement Endowment Trust. We have expended a good deal of our budget this year and I'll explain why in a minute. We're looking to a contract with the Oklahoma State Department of Health. They have some additional funding from the CDC that we can put to what I'm calling overflow call volume, or more than expected demand. And also, they're starting to receive some of the tax dollars from the new tobacco tax, and we're hoping to put a good portion of those to the helpline as well. The demand has been increasing pretty steadily. The service is actually provided by Free and Clear, Inc. They were originally a Group

Health Cooperative of Puget Sound and have since spun off into their own company, and Free and Clear was what they called their tobacco cessation product. Free and Clear is one of about three vendors nationwide that just really, this is their focus, and they've done this for since the early '90's. When they were part of Group Health Cooperative, that entity, that HMO invested a lot in all kinds of systems change in addition to the helpline, and they were actually able to reach the year 2010 healthy people objective in terms of smoking prevalence among their population by actively engaging the physicians and health care providers in addressing this with their patients, referring to the quit line and offering some community services as well. We at the Tobacco Settlement Endowment do not have a large administrative budget and we really are trying to maximize the services that are already available, trying to avoid duplication, so we also have a relationship with the State Health Department, and that's where Linda Wright-Eakers comes in. She actually has the day-to-day responsibility of dealing with the helpline vendor on a variety of issues from how to tailor the client materials to any complaint calls that may come in and that sort of thing. And then we're evaluated by the University of Oklahoma College of Public Health, Dr. Laura Beebe. The hours of operation are 7:00 a.m. to 11:00 p.m., seven days a week. Those hours have expanded to this current schedule within this past year. They do offer voice mail from 11 to 7 and they have some I think, automated messaging if people want to listen in, but all of the messages are returned within 24 hours if at all possible, if they can actually contact the person. The helpline helps everybody, tobacco user, whether they're cigarettes, spit tobacco, whatever form of tobacco. Certainly pregnant smokers, former smokers, healthcare providers, I think this is one piece of the service that's been relatively underutilized. If physicians or other health care providers need assistance with dosing or just basically, how do I help my patient with quitting, the help line's available for that purpose as well. They have a strong science advisory committee, a medical director on staff, and they're quite capable of assisting. And then also friends and relatives of course, you might imagine we get several calls from friends and relatives who are interested in helping someone quit smoking or using tobacco. I mentioned the one call, and the way Linda has it divided here is levels 1, 2 and 3. So basically, level 1 is your typical information referral. If somebody really doesn't want to engage in the counseling process, they're not ready to quit, maybe they just want self help materials or a referral to the community. We can provide that. The single in-depth intake and counseling is approximately a 40-45 minute session with the person. Help them set a quit date, establish a very brief quit plan, get the basics completed with the person. Many times people will engage in that first session and then decide they want to go ahead and complete the rest of the program. But there are quite a few people who just prefer to do the one-time session. And then the intense intervention I've described before is the five active calls. Why a helpline? They're effective in increasing quit rates. They increase reach, and I think that's one of the greatest things about it. You know when you talk about this impact formula of your efficacy of a program X your reach of a program = your impact, so when you think about a class that may serve ten people, maybe three of them quite because they've got a 30% efficacy rate, then your impact is three. But you multiply that by a 1000 or 10,000 like the helpline can do, and you can really have a huge impact on the health of your population. It removes all of the typical barriers in terms of transportation, child care, and I think the other piece is that confidentiality or a level of anonymity that's provided over the phone. Some people just aren't comfortable in a group setting and maybe don't, if they're like me and they work all hours of the day and night, they don't have time to go somewhere at 7:30 every Tuesday night to hear a similar message. And then, they do allow for very improved quality control. Our vendor's one of the top in the country as I mentioned, and they're able to take calls, listen in, supervisors can listen in and offer direct feedback right away when there are problems. For example, we had identified a client who had Medicaid and was referred for her pharmacy benefit and I think she was told that it would count against her typical monthly benefit, so once we were able to identify that, we could call the helpline, they could do another training with the staff just to make sure everybody has the right information and so forth. So it's real easy to follow up and correct any gaps or problems that we find. We did find in one instance where a woman had called the helpline, was referred for her benefit, but then I think she was told to call the SoonerCare helpline number and anyway, she got a variety of different pieces of information from a variety of sources and one thing we learned was there was a computer glitch in the system, so anyway, we've got all that stuff straightened out and the Health Care Authority has too, and I think people are getting the services that they need right now. Cessation is more cost effective than mammograms, PAP smears and many other preventive services that we just routinely provide. Most of us wouldn't dream of having health insurance that didn't cover these basic services, and yet most of our insurance coverage does not provide effective tobacco dependence treatment. And then Oklahoma helpline is averaging a cost of approximately 1200-1500 per quit smokers, so think of all the people that are calling in and then what it actually takes per quit smoker. And I mentioned the impact formulas, so you've got it there in your slides. I won't go through it again, but we can certainly help quite a few more people through the helpline, we can get word out about it and it's a great resource. Just in terms of some brief evaluation information, you'll notice that this is divided by the one call and the five call, so these are people who've actually completed a least one call or who have completed at least some of the five calls, if not all five. So you can see satisfaction varies by the level of service they get. If they're in that five call program, they're all into the 90's, quite happy the service has met their expectations and they'll recommend it to others and it's not even so bad in the one call. But it's about the level you might expect. Now I want to point out that this is data from August of '03 through July '04. That was our first year of operation. We were not providing any nicotine replacement products for the uninsured or the Medicare population as we're trying to do now. So that the, a lot of the dissatisfaction that's come from the helpline has been you know, where are my drugs, why aren't you providing this NRT, because they're not always so enthusiastic about just getting counseling. So I expect the satisfaction rates to go up, although you have to be in the five call program to get the other benefit. The quit attempts, the six month follow up, we ask two basic questions, and it's a point prevalence for seven days and point prevalence

for thirty, so essentially, six months after they've completed their one call or their five call program, we're saying have you had a cigarette, even a puff in the last seven days? Have you had a cigarette, even a puff in the last thirty days? So these are the results. So you can see that among the five call participants, we've got a 29% quit rate with a 7-day point prevalence and 26% at 30. That's average or above average, well above average, for most quit lines across the nation. Certainly, it's far better than self help, which tends to be anywhere from 4-10% with people who will quit on their own.

Dr. Whitsett: *Do you know how many of these people who have maybe quit before? It this a second or third attempt?*

Ms. Strader: *We do have that information. We don't have it in an evaluation, so I don't have it. But we're collecting so much data, we should be able to generate a telephone book size evaluation report. Most people have tried more than once, generally speaking. The quit attempts in the 12-month follow up, so that's six months. Twelve months out, what we're finding is 25% reported seven or more days and 26% have been abstinent thirty or more days, although somehow or other that doesn't make sense to me, because it should be the other way around. But what I think is really interesting is if you go back to the six month follow up, you notice the 17 and 16% in the one call program, and then when we go to the twelve month follow up, it's 19% among the one call program, so there seems to be this little sleeper effect. We've been watching it over the course of that first year and it'll be interesting to see if that trend continues. Then call volume data. I just to give you an idea, you know we've had the clean indoor air policy go into effect a year ago, then certainly the tobacco tax has come into play, beginning January 1, so you can see that we were really doing very little to promote the helpline at all. Just word of mouth. We were offering just the counseling and so forth, but by November, we had the Great American Smokeout and we did a press release, and there were some community events, so that gave us the call spike. And by the way, registered callers does not include people who've called just for general information, hang-ups, pranks, all that. These are people who said, I want counseling, either the one or the five call program. So it's the most conservative number we can offer. In December, that number was down to 1376, but by January, we did a press release on December 27th, something about New Year's resolution, tobacco tax, Philip Morris is increasing their prices too, helpline is here to provide services, and got 2400 callers in the month of January. That was the most in any given month from any given state that this vendor's served, and they serve eleven states right now, plus quite a few commercial clients. Then by February it was down to 1500. And I don't have the March numbers. I tried to call but my client services manager is on vacation today. But all that to say this is primarily word of mouth, so it's really catching on in terms of people hearing about the service from each other, and you know, for us, we do one press release, a few newspapers and television stations pick it up. The Health Care Authority's done a great job about putting it in newsletters and trying to get the word out to their providers and participants, so it's certainly taking off. If we did even a little bit of promotion, paid media, I think the call volume would just be out the roof. And that is what most states experience. Most states right now are service at or below about 1% of their smokers. We're hitting about 2% now. The state of South Dakota did a kind of free NRT for anybody who registered for services, even if they were insured which we can't possibly afford, and they were able to get 10% of their smokers in one year. So it's quite effective if you provide the right combination of services and do just a little bit of promotion. And that's all I have. Questions?*

Dr. Whitsett: *It's an excellent program and one of our challenges is how could we best utilize that. I don't know what we're capable of doing relative to our clientele. Do we have any idea what percent of smokers...are there surveys that have been done among the Medicaid?*

Ms. Strader: *Typically we estimate about 30 to 40% of Medicaid participants are smokers.*

Dr. Whitsett: *And the general population?*

Ms. Strader: *About 25%.*

Dr. Graham: *Do you see bleeps in your calls whenever, like, I know the University's going to go smoke free in July, when you have these institutions and things like that?*

Ms. Strader: *We do. It depends on how well they promote the service and that's a part of Linda's job, is she's worked with the Department of Corrections when they went to the smoke free campus and with Oklahoma City area hospitals and so forth, so depending on how well the institution really promotes it, I think a lot of times people don't know what a helpline is. Free and Clear's just produced a new video that I'm very excited about. I think that'll help give everybody a comfort level with exactly what it is they're getting into when they refer someone. But a lot of times they're just thinking it's information and referral and you can get that anywhere. So if they really understand what it's about I think we do get a little bit of a blip.*

Dr. McNeill: *Are you familiar with the limitations I see at the Health Care Authority on how many smoking cessation products you could get within a year. I don't remember what they are. Given the number of times it takes someone to finally quit, are you happy with that or should that be something we look at removing, given not only that, but the fact that for years the number of smoking cessation products that were reported to us that were utilized were almost meaningless.*

Ms. Strader: *Actually we work together to discuss the benefit and the very first time is what I call a freebie, which is it's not, there's no pre-auth, it's not tied to counseling. You can just get it with a prescription and that's that. So that's wonderful. That's what the public service, public health service guidelines recommend is that people have access to all the products all the time, access to counseling with minimal costs and those kinds of things, so that first one being a free ride, I think is wonderful. You know in terms of cost containment, I think if you're tying that second one to counseling, that's probably not a bad strategy, but if you've got the resources and you can do it, you can always run it as a pilot and just see, you know. But certainly I would say the more you can offer free or at very minimal cost, the*

more barriers you can tear down, the better. You're right. It takes many more times than once and we certainly don't have the resources with the Endowment to be able to provide everything, and one of the things I used to think is well, if everybody else will provide the products, then we can provide the counseling, but what I'm learning is that really we need about two dollars for counseling for every one dollar that is spent in NRT. So we're actually going to eventually if this thing grows as much as I think that it can, we're actually going to really need the health insurers to participate with us and many states really have a good cooperative arrangement like that, so they're not just dependent on one funding source to be able to provide the counseling or the NRT. The one thing I really want to say on behalf of the Board of Directors with the Tobacco Settlement Endowment is, thank you all so very much for encouraging, promoting and covering this benefit. Not many states have really gotten into Medicaid coverage to the degree that we need to see happen. There are a few that cover the full range including the counseling, but to cover all five first line pharmacotherapies with just the prescription and removing all the barriers, that's, it's absolutely a huge step forward, and in these days of limited resources the payoff will be there in the end in terms of the health care benefits. But it's a fabulous step forward. We see it as a great partnership with the Health Care Authority, very, very grateful for you doing that.

Dr. Whitsett: *I know you've pinpointed women in pregnancy. I don't know if you have any special access to them, other . . . OB doctors . . . do they help you promote anything?*

Ms. Strader: *The Smoke free Beginnings Project, I don't know if you all have heard about that, but the Oklahoma State Medical Association had applied for and received a grant from the Robert Wood Johnson Foundation and they're actually going into physician practices. They've got residencies, private practice, group practice and so forth, and they're doing a lot to really work with the physicians. What we find is that it, provider education alone is a waste of energy. But if you can get those reminder systems in place within the office so if you've got an electronic medical record, then they help make the tobacco dependent's counseling, or the ask and the advise and so forth, part of that record, and those kinds of things are helping. We have seen that the vast majority of our fax referrals are from providers that are in that Smokefree Beginnings Project.*

Dr. Whitsett: *Is that limited to pregnancy?*

Ms. Strader: *The Smokefree Beginnings is. The fax referrals can be used for any patients.*

Dr. Whitsett: *The diabetics are the ones that I see in the area I work in, so riddled with vascular disease . . . Ridley says, should be against the law for diabetics to smoke and maybe it should, but I'm not going to go out and promote that. But on the other hand, maybe there's something that, among individuals that we know who are diabetic, making them aware . . . may not be smokers, some of them are. Making them aware of the special services that could be available to them. It's just, I don't know if there's anything that would be appropriate to do, but something to think about, because that is such a serious combination, deadly combination.*

Dr. Bell: *How young are clients?*

Ms. Strader: *How young? Eighteen and above. According to Oklahoma state law, we can't provide the counseling without parental consent and over the helpline, I'm not saying we can't go there, but I think it would be very difficult to get written parental consent to get somebody engaged. We've taken a look at it, but you really, if the helpline counselors were nurses, physicians and others as defined as a healthcare professional in the state law, we'd be okay, but most of them have you know, a master's degree or bachelor's degree in some kind of behavioral health field.*

Dr. Whitsett: *Is that true for birth control in Oklahoma?*

Ms. Strader: *No, I don't think it is, as a matter of fact. Birth control is being provided by a healthcare provider, so that's the difference. You know, CMMS has just covered tobacco dependence counseling for Medicare patients, and then of course the drug benefit will kick in in January, but they are not yet covering telephone counseling for tobacco dependence treatment because there's something in their policy that these engagements have to be face-to-face. So that's been kind of an uproar among the helpline community, is really trying to get people the access to the services. Given the resources, though, I will just mention some of the original research was done in Dr. Prochaska's shop in Rhode Island where he had a contract with the health maintenance organization that turned over the entire client list to the helpline and they called each one to both, one, to identify their smokers and then, two, offer the services. And it was hugely successful in terms of participation and quit rates.*

Follow up information: Spanish help line: 1-800-793-1552; July 2004 through March 2005: 930 Medicaid/SoonerCare clients registered for counseling.

Materials included in agenda packet; presented by Dr. Gorman. Dr. Whitsett asked if Zyban's manufacturer still provided the help line as a service to Zyban users.

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 6: 30-DAY NOTICE OF INTENT TO PRIOR AUTHORIZE ANTIDEPRESSANTS

For Public Comment, Courtney Walker: *Good evening. My name is Dr. Courtney Walker and I'm with the outcomes research department at Eli Lilly and Company. I would like to thank you for this opportunity for me to come and speak a few minutes to you concerning Cymbalta®. Cymbalta® is a selective serotonin and norepinephrine reuptake inhibitor that is indicated for the treatment of major depressive disorder and it was the first drug indicated for diabetic peripheral neuropathic pain. Although the exact mechanism of depression is unknown, our substantial body of research has shown that serotonin and norepinephrine play a major role in the symptoms of depression, in the cause*

and the maintenance of depression. In addition, depression has been strongly linked to painful physical symptoms associated with it . . . oh excuse me . . . computer . . . specifically joint pain, back pain, other types of body aches and pains. And many depressed patients in primary care settings present to their physicians with painful physical symptoms. There was a study done in '99 by Simon which says that 69% of their patients presented to their primary care physician with painful physical symptoms. In treating depressed patients, remission should be the goal of therapy and failure to reach remission can result in a threefold increase in risk of relapse, a threefold decrease in time to relapse and increased utilization of medical services. With so many treatment options available, of course there's a lot of drugs available for depression, the majority of depressed patients achieving only partial recovery of symptoms, partial recovery has been linked to greater numbers of relapse. It is important to highlight the unique attributes of Cymbalta® in the treatment of depression. Again it is indicated for major depressive disorder, first drug indicated for diabetic peripheral neuropathic pain. It is a selective serotonin and norepinephrine reuptake inhibitor with nearly equal affinity for both serotonin and norepinephrine. When you think about . . . it's a dual action SSNRI, how does that mechanism of action work? Cymbalta® mediates the core depressive symptoms in the brain and also it regulates somatic symptoms in the descending pain pathway of the spinal cord. In two once daily 60 mg clinical trials . . . excuse me . . . as early as week two, Cymbalta® significantly improved major depressive disorder as measured by reduction in the Hamilton D-17 total score. As early as week one there was significant improvement in depressed mood which is item one of the Hamilton D-17 scale. And as early as week five Cymbalta® significantly separated from placebo with remission rates of 45% compared to 16% for placebo. In a 52-week long term study, 82% of Cymbalta® treated patients reached remission. Painful physical symptoms with depression were also studied in the clinical trials. As early as week two, Cymbalta® significantly improved overall aches and pain in depressed patients as measured by an improvement in the VAS 100-point scale, which is a visual analog scale, it's a hundred meter line, one hundred is worst pain possible, zero is no pain at all. As early as week one, Cymbalta® significantly reduced that pain associated with depression. In clinical trials for diabetic peripheral neuropathic pain, Cymbalta® showed significant improvement in pain severity as early as week one and also it continued throughout the twelve weeks of the diabetes studies. There were two 12-week studies that took place. In addition, Cymbalta® was effective on relieving pain at night in patients with diabetic peripheral neuropathic pain. It has a favorable safety profile and is well tolerated. The most common adverse effects are nausea, dry mouth, and constipation. No significant incidence of hypertension and no QTC prolongation were noted in clinical trials and it's also weight neutral. Also there's a low incidence of sexual side effects. Again, it's a selective serotonin and norepinephrine reuptake inhibitor that is indicated for major depressive disorder and also it was the first drug indicated for diabetic peripheral neuropathic pain. A high percentage of patients reached remission which could translate to sustained treatment gains and reduce the reduction in utilization of medical services. I'd be happy to answer any questions at this time.

Dr. Whitsett: *What about weight changes?*

Dr. Walker: *There was an 8-9 week study done. There was also an 8-week, 8-month study done, and it was found to be a weight neutral drug, so there was no increase, no significant increase in the weight as a result of taking Cymbalta®.*

Dr. Whitsett: *Drug interactions?*

Dr. Walker: *Drug interactions . . . it is metabolized via 2D6 and also 1A2. It is a moderator inhibitor of 2D6, not as much as a fluoxetine but more so than desipramine, so drug interactions are with benzodiazepines, TCAs, some SSRIs, also with 1A antiarrhythmics as well.*

Dr. Whitsett: *And the range in dosage on an average is what?*

Dr. Walker: *40-60 mg, and the package insert states 20 mg twice a day, and 30 mg twice a day, so the range is 40 to 60 mg, qd. And the clinical trials mainly were 60 mg qd.*

Dr. Whitsett: *The rough cost, AWP or whatever you want to use for this medication?*

Dr. Walker: *Around $3.35, around $3.35 AWP, per 60 mg capsule I do believe.*

Dr. Nesser: *Is it flat priced, do you know?*

Dr. Walker: *It is flat priced.*

Dr. Nesser: *So it doesn't matter if it's a 20, 30 or a 60?*

Dr. Walker: *Doesn't matter, doesn't matter, but indications are using 60 mg qd, 30 mg for individuals who have tolerability concerns.*

Dr. Nesser: *So it's almost $7.00 a day.*

Dr. Hollen: *$7.00 a day, I'm sorry ... how are you getting that?*

Dr. Nesser: *Two . . twice a day.*

Dr. Hollen: *But that's really not how it's indicated.*

Dr. Nesser: *He just said it was 20 or 30 bid.*

Dr. Walker: *40, 40, yeah . . 40-60 mg qd. But 60 mg qd is the flat dosing. That's what (unintelligible) 30's and 60's also . . . there are 20's, but it's mostly 30's and 60's. You have to special order to get the 20's.*

Dr. Whitsett: *So if a patient's taking 60 a day, once a day, or does he take 30 twice a day?*

Dr. Walker: *60 mg qd.*

Dr. Whitsett: *Once a day? Not a twice a day dosing?*

Dr. Walker: *Once a day. Just 60 mg qd, that's dosing. But I was just telling you how the package insert had it stated.*

Dr. Hollen: *The package insert is different from actual use and actual (unintelligible).*

Dr. Walker: *The package insert just states, if you've seen it, I didn't know if you had it in front of you, says 40 to 60 mg qd. The standard dose though is 60 mg qd.*

Dr. Whitsett: *Once a day dosing.*
Dr. Walker: *Once a day.*
Dr. Whitsett: *So that could be $3.35 per day.*
Dr. Chonlahan: *Is bid dosing for tolerability, is that right?*
Dr. Walker: *Tolerability, if there's a person that has a problem with nausea or taking the medication.*
Dr. Chonlahan: *Is the dose dependent . . . adverse effect?*
Dr. Walker: *Adverse effects, there were studies done in terms of looking at 60's and 30's. There was more nausea with the 60 mg than there was with the 30 mg.*
Dr. Chonlahan: *So bid dosing would be . . .*
Dr. Walker: *. . . would be better for an individual who would be susceptible to nausea, but at the clinician's discretion they can choose to tell, you don't have to take it with food, but food of course may quell that nausea.*
Dr. Whitsett: *It does not have a black box warning?*
Dr. Walker: *For suicide . . . all the antidepressants do.*
Dr. Whitsett: *Age recommendation.*
Dr. Walker: *Clinical trials were 18 to 65, so all the adults.*
Dr. Nesser: *And do you have any head-to-head comparisons with another antidepressant?*
Dr. Walker: *Imminently approaching, so nothing right now, nothing right now.*
Dr. McNeill: *(abbreviated) If you only have one drug that's indicated for neuropathic pain, how can you get there by going through a tier-2 drug first?*
Dr. Nesser: *That would be number 4, approval for a unique indication.*
Dr. Bell: Do you have on-going studies with tenagers.
Dr. Walker: No, not at this time.
Dr. Bell: Any published university studies?
Dr. Walker: No.
Dr. Hollen: *Can you clarify the 30 and the 60 mg dosing and the nausea and the tolerability study?*
Dr. Walker: *In terms of again, the dosing, the indication is 60 mg qd. The package insert does say 40 to 60 mg and in parentheses it has 20 mg twice a day, 60 mg has 30 mg twice a day. In the study it just looked at nausea because of course a lot of the drugs that deal with serotonin, there is the increase in nausea when you do take those medications, and at 60 mg there was more nausea than at 30, but it is again, it's a transient nausea that usually is gone in a week.*
Dr. Le: *Should there be any instance where a client is on BID dosing after 3 to 6 months of therapy?*
Dr. Walker: *No, again the nausea was transient, it only lasts a week to two weeks.*
Dr. Gorman: *But there's no 40 mg dosage for it, right?*
Dr. Walker: *No, but most of our physicians, over 85% of the scripts are 60 mg qd. That's just how the package insert reads.*

For Public Comment, Dr. Joe Rippager: *I just want to thank the DUR Board for allowing me to talk about my concern. I wanted to just let you know that I, as I reviewed the page where the tier-1, tier-2 antidepressants are listed, that's the page that I'm on, I'm going to be referring to that page throughout my presentation. As I was looking at that, one of the main concerns that I have, and I'll go through a little more detail of why I'm concerned about that, but one of the main concerns that I have is that the two SNRIs, mainly duloxetine and venlafaxine are both on tier-2, which means there's really no SNRI available on tier-1. To be a little more specific, as I looked through this and noticed that of the, of all the newer generation antidepressants, let me give a little background to me. I'm a psychiatrist in Norman, I've been in practice for about ten years and I treat probably 80% of what I do, I see about 60 or 70 patients a week and about 80% of what I do is antidepressant treatment for mood disorders. So these are the medications that I use the most, and one of the things that I wanted to point out is that of all the newer antidepressants that are listed, and I'm not including the tricyclics or monoamine oxidase inhibitors, only about three on this list are in tier-2 and they are duloxetine, venlafaxine and then bupropion, Wellbutrin® XL . . . XL being once a day, which distinguishes it from the tier-1 bupropion because you have to give them twice a day. And as we look at the antidepressants that we're using, those three are probably the most popular antidepressants that we're using as psychiatrists. Now among primary care they're not. Many of the primary care doctors are not going to have any problems with this arrangement here because they mostly use SSRIs, but most psychiatrists use the SNRIs and we use Wellbutrin, preferably the once-a-day, but one of the reasons we use the SNRIs so often is because the literature supports and confirms that there's evidence that they can be more effective when it comes to remission. And in fact if you categorize dual action antidepressants, you'd really include tricyclic antidepressants in that category because most tricyclics with the exception of two are dual action antidepressants. What you're really coming down to are two groups, dual action antidepressants and single action antidepressants, and so when we look at dual action, this arrangement that you have here with tier-1, tier-2 implies that the tier-1 are equivalent to the tier-2, and that is just simply not the case. I mean the tier-1 dual action antidepressants that are listed, specifically Remeron®, Desyrel® and Wellbutrin®, really only one of them is commonly used, and that's the Wellbutrin®. The Remeron® is not used much because it has so many side effects. It's a great dual action drug and it's very well received in kind of a niche group, in which is patients who don't care if they gain weight or they don't, or they're having problems sleeping. Generally we will use Remeron® in elderly patients who are not eating, but it's not used hardly at all because of its' tolerability. And the trazodone is so sedating that most psychiatrists use it just for sleep and usually at low doses, so that drug really is not used much*

either. So the only one on tier-2 are the dual action drugs that you're going to get people to actually use are the Wellbutrin®, and that's going to be twice a day.
Dr. Whitsett: *What was the issue with bupropion's sustained release?*
Dr. Rippager: *Well it's twice a day. The studies show that the more times a person takes a drug, the more times they're going to miss that drug, so a lot of people who take, say Wellbutrin®, twice a day, they will miss their second dose, then they end up with subtherapeutic doses. So once a day drugs are always better and in fact, most twice a day antidepressants have never done well on the market because there's so many once a day antidepressants. So I guess my point is that of the antidepressants in tier-2, specifically duloxetine and venlafaxine, I would hope that they would be moved to tier-1, because really there's nothing comparable to be able to give our patients in the tier-1 category.*
Dr. Graham: *I have a question. Cymbalta®'s has just now came out, hasn't been out very long, probably . . . what did you do before these came out?*
Dr. Rippager: *Cymbalta®?*
Dr. Graham: *I'm talking about the SNRI's . . . what did you do before now when these drugs were available. How did you treat your patients with these . . .*
Dr. Rippager: *Venlafaxine's been around quite a long time so we've had that since the mid-90.*
Dr. Graham: *Did you use that specifically then, or did you use . . .*
Dr. Rippager: *Effexor®? Yeah we used it, we used it. If you say, well what did we use before Effexor®? We used the SSRIs and if that failed, we went to tricyclics because tricyclics are next SNRI, I mean they're not, I shouldn't say that. They're dual action, they're not SNRIs, they're dual action drugs and they have better efficacy really when you look at studies than the SSRIs, much better efficacy. The reason we don't use them is because they're not safe and we're afraid that there's so many overdoses on a tricyclic, and they had access to an SSRI, then we could be sued. So most people won't give, psychiatrists won't give tricyclics to anybody who they think is at risk for suicide; whereas with venlafaxine and now Cymbalta®, that suicide risk is no longer there. So if you look at SNRIs, the thing that's so neat about that drug class is you end up getting the efficacy that we used to get with tricyclics and the safety profiles that we now have with SSRIs. You get the best of both worlds.*
Dr. Gourley: *Primary care physicians probably wouldn't have trouble with the tiers, but that you as a psychiatrist wanted access to the tier-2 drugs. Do your patients come by referral or . . .?*
Dr. Rippager: *Not always. We get a lot . . . depending on how . . . you know, what I've noticed the longer I'm in private practice, the more patients come to me that have never been treated. You know, initially yeah, it was almost, first couple of years, it was almost all by referral because nobody knew I was in practice, but once you get in practice and you start having a network of patients that you've treated, now you've got people coming in without referrals. I'd say 75% of my patients don't come through referrals.*
Dr. Gourley: *And they're the Medicaid patients that we're talking about?*
Dr. Rippager: *Well I have a lot of patients who have Medicaid as a secondary because I treat a lot of Medicare patients. So they're not Medicaid in the sense that that's their primary insurance, but they get their medicine from the Medicaid program.*
Dr. Chonlahan: *You say once daily dosing is better, didn't you say once daily antidepressants, there is numerous . . . which one were you referring to?*
Dr. Rippager: *Well what I was saying is that Wellbutrin® XL is a once daily bupropion and the Wellbutrin and the Wellbutrin® SR is a twice daily, so the tier-1 are twice daily, tier-2 is once daily.*
Dr. Mitchell: *The population you treat, primarily being the adult population, as we all know, come January 1st, they won't be receiving their medication through us anymore, just so that's clarifying for the Board, because Medicare Part D actually takes over the responsibility for the medication on January 1st.*
Dr. Bell: *This is a comment. I'm going to tell you as a Board member, the child literature is really excited about the SNRIs because what you see so often as a child psychiatrist, you see children and teenagers, they hate the numbing, the disinhibition, so you really, if you get that which you often do, you're excited about these dual reuptake inhibitors, and a lot of my patients I cannot afford two failed trials on the tier-1. I mean maybe I'll have the third suicide attempt or whatever, so it's a little worrisome to have to have two failed trials on tier-1 before I can move.*
Dr. Rippager: *I would agree. The problem with that is that patients don't stick around that long. If they fail two drugs, they really don't want to come back. The other thing about the point that Dr. Bell's making is a very good one, and the literature now is coming out about this, and it's more and more going . . . I think it's more and more going to be relevant, and that is that long term SSRI treatment does cause an emotional numbing and it is real and patients do describe it and the only way to avoid it is to have dual action drugs and you can get that through Wellbutrin® and you can get that through the SNRIs, so that's a whole separate issue that he's bringing up. That hasn't really been addressed and we're going to see that more and more as a problem when you limit those, when you limit these drugs. I'm telling you the ones you have here on the dual action first tier, they won't be used. So everybody will be using the SSRIs and that means people are going to have to fail two SSRIs before they ever get to the dual action, the really good dual action drugs.*
Dr. Chonlahan: *Is there any relapse with the dual acting antidepressants?*
Dr. Rippager: *Relapse? Is the relapse different than SSRIs? Well that's currently being studied and I don't, I think you can find studies that would show both ways. And the gentleman that came up for Eli Lilly laid it out nicely and that is that the . . . relapse rates are much higher when you don't get to remission. And there is data, a lot of data that demonstrates that the dual action drugs take people, more people to remission than the single action drug (TAPE*

END). There's no doubt in my mind that dual action drugs take more people to remission and there's less relapse. No doubt in my mind, and I've felt that way for a lot of years, six years, which is why I've been excited about Cymbalta® coming out because now we've got two instead of one.
Dr. McNeill: *Is the time of onset of tier 1's and tier 2's pretty much the same or the relief of symptoms?*
Dr. Rippager: *Depends on who's asking?*
Dr. McNeill: *Well, I'm asking you. I'm not looking for an evidence based answer. In your practice . . .?*
Dr. Rippager: *In my opinion, the tier, my opinion the SNRIs work faster than the SSRIs, so my experience if you, if you, you know, I don't think Remeron®, I think Remeron®'s a fast acting drug, too. The problem is, it's not used. So when you asked me well are the tier-1 shorter, I mean, take longer to get to remission, well, not necessarily. I think we'd have to clarify which ones in tier-1 you're talking about. If you're talking about the serotonin reuptake inhibitors, my opinion is that the SNRIs take you to remission quicker.*
Materials included in agenda packet; presented by Drs. Le and Chonlahan.
Board members discussed College of Pharmacy recommendations and change proposals to recommendations. Dr. McNeill stated that he would like to see 4 weeks limited to tier 1 trials. Dr. Bell stated that he would like to see an exception statement added to the criteria for physician specific exception requests. Dr. Whitsett asked for the COP to bring these two changes to the current recommendations brought back to the DUR Board for an action item.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 7: ANNUAL REVIEW OF ANTI-ULCER PRODUCTS
Materials included in agenda packet; presented by Dr. Chonlahan.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 8: ANNUAL REVIEW OF XOLAIR®
For Public Comment, Kristi Robinson: *Good evening. I've been taking the Xolair® injection now for probably about a year and maybe a little less. At first I was on steroids all the time for about five years, maybe three weeks out of the month, and allergies and asthma were horrible. Many other medications . . . I was off work a lot. I was in the emergency room all the time. On a nebulizer, many inhalers and now I've gotten down to where I'd say in the past four months, have been on the steroids once, maybe for a week. My asthma attacks haven't been as serious and haven't lasted as long. I work with animals on a daily basis which plays a big part in how that injection works for me. Even co-workers have noticed a huge, huge difference in how I'm able to function, mainly with cats. Where I would normally have to take several allergy pills to get through the day and what have you, I don't have to do that anymore. Just the minimum. My home life has been wonderful since I've been on this injection. I can actually enjoy my child instead of you know, instead of a weekend event, being in shock because we have to go to the emergency room, that's all been curtailed. I feel like I'm really under control with this. Everything's under control. I have got several animals at the house, several in the house. A lot of people would find that to be odd because I do have allergies and asthma. Living and existing are two things that I weigh a lot and the Xolair® injection has allowed me to live, not just exist, with the things that I like. So I guess maybe, I really just wanted to take this opportunity and tell you guys just how wonderful it's worked for me. I feel like I was in just a really deep, deep, deep rut with allergies and asthma, but yet I wanted to live with the things that I loved. I wasn't for sure if I was going to be able to do that, but with this injection, I've just done wonderful, absolutely wonderful. I've quit gaining the weight because I don't have to take the steroids anymore. That was a huge part, huge. So I would just like to say thanks. Thanks for letting me talk about it. It's been wonderful.*
For Public Comment, Evie Knisely: *Good evening. My name is Evie Knisely and I'm a Regional Account Scientific Associate Director, a long title, but I'm with the scientific operations division of Novartis. I want to talk to you tonight about the PA criteria that's been proposed for Xolair®. Specifically, number 2 and number 8. Number 2 is the requirement for patients to be severe persistent only and number 8 is the requirement for two hospitalizations and two ER visits in a six-month period, one of those being in the last 30 days. Xolair® is the first humanized therapeutic antibody for the treatment of asthma and the first approved therapy designed to target the antibody IgE. It is co-promoted by Genentech and Novartis, in case you're wondering and thinking it's a Genentech drug. Their sales force promotes it but Novartis is supporting it on the science side. I want to call you attention to the packet, the handout . . . the P&T Journal article that you've been given, and that article was published in June of 2003 and it is a consensus guideline piece that was put together by experts in asthma. Doctors Lanny Rosenwasser of the National Jewish in Denver and then David Nash who is at Thomas Jefferson University Hospital in Philadelphia, and they lead a distinguished group of asthma experts, and they've put together this consensus guideline. Now I'd like to call your attention to page 407 of that particular article and if you'll look at that particular page, what you'll see is that they have designed an approach to the management of asthma and they have listed their considerations for IgE blocker therapy, and you'll see that that consideration applies to both severe persistent and to moderate persistent patients. There's also no evidence, if you read their recommendations, there's no requirement or no evidence of a need for hospitalization or ER visit. So again, I'd like to reinforce that this particular consensus panel does not require an ER or a hospitalization visit and they also recommend the use of an IgE blocker, Xolair®, in patients who are also*

moderate persistent as well as severe persistent. I'd like to contrast that with your particular requirements for diagnosis of severe persistent asthma only. And also your requirement is that patients must have been in the ER or hospitalized by asthma exacerbation twice in the past six months and once in the last thirty days. And we understand when you created these guidelines that the drug was new, had no experience with it, it was expensive, it was coming on in the market, you had no idea whether there was going to be a lot of utilization and you had no idea whether or not Genentech and Novartis were going to promote this drug appropriately. I want to allay any fears that you might have that Genentech is detailing this drug with only allergists and the pulmonologists, so specialists only. They are not doing pediatricians and not doing family practice and they're not doing general practice. We think that specialists are the only doctors who have the comfort level or the expertise to treat these patients and to give these patients the appropriate level of care that they need. I wanted to bring your attention to three letters from Oklahoma physicians, specialists in Oklahoma who were not able to come tonight but that wanted to have their voices heard. And again, these are practicing specialists in the State of Oklahoma. The first letter is from a Dr. Overholser and if you'll look at the last paragraph, paragraph five, I can read the letter for you. It says that "Due to the variability of the disease, I do not feel, however, that two visits to the hospital or ER in a 6-month period is a necessary requirement. At the very least, a visit in the last 30 days should absolutely not be required. Many times it may take longer than thirty days before a patient could be scheduled to be seen by a specialist". So they're arguing against that 30-day component because it takes longer than that to get the patient in to see a specialist. The next letter is from Dr. Purser of the Allergy Clinic of Tulsa and I call your attention to the second and third paragraph, and Dr. Purser states that "Our ability to use nebulizers and medications have greatly reduced the hospitalization rates and rarely do we require a hospitalization for management of even severe exacerbations. The use of oral prednisolone alone is a very powerful anti-asthma medication yet it has very severe consequences. Many of these patients stay out of the hospital by taking oral prednisone on multiple occasions if not daily". I think that was testified to by our last speaker. "This particular criteria to require hospitalizations would not identify those patients who have allergy induced triggers but instead identify only those individuals who seem to have difficulties in following medication directions, i.e., compliance issues, and perhaps might identify the elderly or the very, very young who cannot keep fluids down, thus requiring fluid hydration and these are not necessarily the individuals we are trying to look for when we're thinking about prescribing this drug in patients that would derive benefits from the use of Xolair®." Then the last letter from Dr. Love, also of Tulsa, the second paragraph, "Criteria 8 is excessive and unreasonable. In this day and age patients, parents and family can often provide better respiratory care than most hospital floors except for ICU units. Requiring hospitalization criteria will force physicians to hospitalize patients just to fulfill these medical requirements to get Xolair® and result in an increase in cost to the State." And the last point that I would like to make is based on some of the other health plans and other Medicaids and requirements that they have used for Xolair®. Blue Cross/Blue Shield of Oklahoma uses the package insert criteria to evaluate patients for therapy. Missouri Medicaid uses the P&T article that I've given you tonight. Texas Medicaid uses the package insert criteria. So, in conclusion I'm asking that you reevaluate criteria 2 and criteria 8. For criteria 2, appropriate patients would include moderate persistent as well as severe persistent as stated in the PI and it was reflective of the populations in the clinical trials done with Xolair® and as stated in the P&T consensus guideline. And for number 8, decrease or eliminate the requirement for hospitalization or ER visits, and also eliminate the requirement for one of the visits to be in the last thirty days. Any questions?

Dr. Nesser: *What's the cost per patient per year?*

Ms. Knisley: *Well, per month it's going to vary and again as you know, it's dosed on the IgE level and the weight of the patient so that determines their dose. You're looking at $500 to $3500 per month, so there's a range there based on a patient's weight and the patient's dose.*

Dr. Nesser: *Do you think that the physicians who sent letters would be willing to take a rate cut to pay for that therapy for the selected patients who haven't gone in the hospital in order to make this cost effective for the State.*

Ms. Knisley: *I don't know that I can answer that question, I'm sorry.*

Dr. Whitsett: *Do these individuals treat Medicaid patients?*

Ms. Knisley: *Yes. All three. And they've all submitted patients.*

Dr. Hollen: *They've all submitted patients? So the 100% denial . . .?*

Ms. Knisley: *Right. They've all submitted patients and have been denied.*

Dr. Hollen: *It is kind of interesting that none of these patients met the criteria. Am I reading that right? Total physicians submitted in this category during specified time period were 39, approved 0. Nobody met the criteria?*

Dr. Nesser: *It's highly likely. A bunch of them, as you see, were under 12.*

Dr. Hollen: *Oh I thought that 19 went with the actual approvals. Up above that's 19.*

Dr. Nesser: *No, those are ages.*

Ms. Knisley: *Right. Our intention is not to dispute using it in patients off label under the age of 12 at all. We don't want to go there, but we are concerned about the hospitalizations.*

Dr. Hollen: *I would make the recommendation that we go ahead and change criteria 2 to be moderate or severe persistent asthma and discontinue criteria 8.*

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

After discussion, Board members recommended to discontinue criteria 8 requiring hospitalization/ER visits. Dr. Whitsett asked how long do patients usually take this drug? Dr. Whitsett asked what our experience is with Medicaid clients going to the hospital with asthma? Dr. Whitsett asked to bring this item back to the May 2005 DUR Board

Meeting for further review. Dr. Whitsett asked in addition to this possibly bringing in an allergy specialist to address the Board. Dr. Hollen asked to get possibly the Texas utilization on Xolair.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 9: REVIEW & DISCUSS SELECTED NARCOTIC DRUG UTILIZATION

For Public Comment, Alan Barreuther: *Thank you very much for allowing me to be here. My name is Alan Barreuther and I'm a medical liaison for Purdue Pharma. I'm a pharmacist with clinical experience in acute care and patient management and also in hospice experience in palliative care. I am currently employed as medical liaison in risk management and health policy for Purdue Pharma. I'm here this evening to discuss two of Purdue's Schedule II opioid analgesics, OxyContin tablets which are oxycodone hydrochloride and Palladone, hydromorphone hydrochloride extended release. The need for today's discussion is based on current surveys indicating that almost half of all American households, that's 44 million, or 43% . . . that at least one family member who suffers from chronic pain due to a specific illness or medical condition. NIH estimates the cost of uncontrolled pain for our economy at $100 million each year in health care utilization expenses, lost productivity compensation and litigation. In a statement to the US Food & Drug Administration, Anesthetic and Life Support Drug Advisory Committee, Dr. Richard Cain, who was then president of the American Pain Society noted that "For many patients, one drug does not fit all. Studies indicate that 80% of patients may require at least one switch of opioid medications and 20% of patients require three or more switches of medication to manage their pain in the most optimal manner. Even though opioids derive from the same general chemical family, there are clinical differences in the way which patients respond to specific drugs, therefore it is essential to have many opioid medications and formulations available for clinicians to provide the appropriate clinical flexibility that allows optimization of therapy, individualization of the treatment of patients. In addition, a treating clinician needs to take differences in potency, side effect profiles, metabolites from kinetic profiles and delivery systems into account based on individual patient situation." With this in mind, I will now discuss Palladone and OxyContin and encourage the committee to refer to the box warnings and the information I have provided you on the table. Palladone contains the potent Schedule II opioid agonist, hydromorphone. Hydromorphone is an old drug and was first clinically introduced in the United States in 1926. Palladone represents the only FDA approved modified release formulation of hydromorphone, the nature of which allows it to be administered once every 24 hours. Palladone is available in 12, 16, 24 and 32 mg capsules. Palladone is indicated for the management of persistent moderate to severe pain in patients requiring continuous around the clock opioid analgesia with a high potency opioid for extended period of time, generally months or longer. The efficacy of Palladone was established in a double blind randomized parallel group multi-centered placebo control trial, as required by the FDA. The majority of patients experience moderate to severe pain due to musculoskeletal disorders while maintaining and on one or more opioid analgesics, often in addition to non-opioid analgesics (TAPE END). . . where at least 8 mg of raw hydromorphone per day or an equal analgesic dose of another opioid for a week or longer. Use in opioid non-tolerant patients may lead to fatal respiratory depression. Appropriate patients for treatment with Palladone include patients who require high dose opioids on an around-the-clock basis to improve pain control in patients who have difficulty attaining adequate analgesia with immediate release formulations. Palladone capsules are not intended to be used as the first line opioid product prescribed for a patient, or in a patient who require opioid analgesia for a short period of time. Palladone capsules are contraindicated for use on an as-needed basis. The safety of Palladone has been evaluated with over 600 patients with moderate to severe pain in double blind clinical trials. The most common side effects include constipation, nausea, headache, somnolence, ischemia, vomiting and pruritis. Palladone capsules are to be swallowed whole and are not to be broken, chewed, opened, dissolved or crushed. Consuming alcohol when taking Palladone capsules or taking broken, chewed, dissolved, or crushed Palladone capsules where its' contents can lead to rapid release and absorption of a potentially fatal overdose of hydromorphone. OxyContin differs from Palladone in its' modified release formulation, indication, potency, dosing, frequency, and patient population. OxyContin tablets are indicated for the management of moderate to severe pain when continuous around-the-clock analgesia is needed for an extended period of time. OxyContin is not intended for use as a prn analgesic. The safety and efficacy of OxyContin has been studied in moderate to severe pain due to various etiologies such as cancer, osteoarthritis, diabetic neuropathy and postherpetic neuralgia. OxyContin provides an onset of analgesia within one hour in most patients in prolonged pain control allowing q-12 hour dosing. Some of the most common side effects with OxyContin include constipation, nausea, somnolence, dizziness, vomiting, pruritis, headache, dry mouth, sweating, and weakness. Serious adverse reactions with OxyContin are those observed with other opioid analgesics, including respiratory depression which can be fatal, apnea, respiratory arrest, and to a lesser degree, circulatory compression, hypertension and shock. OxyContin tablets are to be swallowed whole and not to be broken, chewed or crushed. Taking broken, chewed or crushed OxyContin tablets leads to a rapid release and absorption of a potentially fatal dose of oxycodone. Approved labeling specifies the controlled release nature of the formulation of OxyContin to be effectively administered every 12 hours, however the labeling does not define a dose of OxyContin in terms of a single tablet strength. It states, as with all opioids, the minimum effective plasma concentration for analgesia won't vary widely among patients, especially among patients who have been previously treated with potent agonist opioids. As a result, patients must be treated with individualization, individualized titration of dosage to the desired effect. The minimum effective analgesic concentration of oxycodone for an individual patient may increase over time due to an increase in pain, the development of a new pain syndrome and/or the development*

of analgesic tolerance. In ending here, at the last paragraph, because the steady state oxycodone plasma concentrations are approximated within 24 to 36 hours, OxyContin dosage adjustment may be carried out if in one to two days. There is no clinical information on OxyContin dosing intervals shorter than q-12 hours as a guideline except for the increase of 10 to 20 mg every 12 hours, the total daily dose of OxyContin can increase 25 to 50%. I guess the thing we'd like to make here is that even though the drug is given every 12 hours, that it doesn't say specifically that it's one tablet twice a day. The titration sometimes will take you to three tablets a day, as we've added in the little colored dosage guideline brochure that we passed around. So I would urge the committee when looking at their guidelines and recommendations to the DUR activities to look at the tablet requirements that have been placed in your current package that you have in front of you. Any questions?
Dr. Graham: *I have one question. Does your patient assistance program pay for three times a day?*
Dr. Barreuther: *I'd have to refer you to the people taking care of that in Stanford. We pretty much stick by the package insert which is q-12 hours.*
Materials included in agenda packet; presented by Dr. McIlvain.
Dr. Gourley moved to accept the quantity limit recommendations; second by Dr. Meece.
ACTION: MOTION CARRIED.

AGENDA ITEM NO. 10: REVIEW & DISCUSS IBS PRODUCTS
For Public Comment, Evie Knisely: *I want to talk to you about Zelnorm® which is Novartis' drug or IBS constipation predominant in females and it is unique in that it treats all the three symptoms of IBS, that being abdominal bloating, cramping and pain. It also is indicated for chronic constipation in males or females. I wanted to specifically with Zelnorm® your criteria for prior auth, and that being the third one which you have a requirement for a prior auth after 90 days. What I wanted to show you in reference to that are two particular studies that you've got in the handout that John just gave you, and the first one is the German retreatment study. This will be on the second page of the handout he just gave you. What this shows is a study that looked at 513 patients. They were washed out for two weeks and then they were put into the initial treatment phase with tegaserod 6 mg bid for 12 weeks, which is the standard dose. And then they were actually pulled off of medication, so a withdrawal period that lasted for two months. Then they were placed back on the medication for an additional four weeks. What we tried to do with this study was look at a real world situation because in the real world we know that this disease waxes and wanes. Patients have remissions, they get better and they quit taking their medication, or they take half a medication. They do all kinds of interesting, creative things. But we don't see patients stay on this bid for a long period of time, so we wanted to design this study to really answer that question, what happens with those patients. On the next sheet, you can see that. In the first group, 85% of the patients were responders, and then when they were pulled off, there was one patient, interestingly enough, that responded in the withdrawal period, but when they were retreated, 88% of the patients responded. So what this shows us is that if you pull patients and don't treat them for awhile, perhaps their disease is in remission. When it comes back we can treat them again and they will still respond and this illustrates the efficacy of the drug. The next page is the LATAM study, or Latin American study, and this was a study that looked at 544 patients. They baseline washout for two weeks, then they were placed on tegaserod 6 bid for four weeks, and then they were placed into either a continuous therapy arm or a withdrawal arm, so one arm had tegaserod 6 mg bid continued, the other study was . . . patients from the other arm, the patients were withdrawn. On the last slide you can see what happened with these patients. The Y axis is the probability of nonreoccurrence of symptoms in patients who are on continuous therapy, and I know you can't see colors, but the top line is patients who were on continuous therapy and you essentially have almost a 100% nonreoccurrence of symptoms for those patients. But the patients that were in the withdrawal arm, as soon as the drug was withdrawn, their symptoms came back, almost to a 30% probability of nonreoccurrence of symptoms. So what these two studies demonstrate is that it makes sense to treat patients for longer than 90 days and we do have data to show you that that is effective. Any questions?*
Materials included in agenda packet; presented by Dr. Browning.
Dr. McNeill moved to accept recommendations for quantity limits and age restriction as presented, motion seconded by Dr. Meece.
ACTION: MOTION CARRIED.

AGENDA ITEM NO. 11: FOLLOW-UP ON BOARD MEMBER QUESTIONS
11A: Diabetes & Hypertension
11B: Traditional NSAID Usage
11C: NSAID Survey Results
Materials included in agenda packet; presented by Drs. Gorman and Flannigan.
ACTION: NONE REQUIRED.

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

AGENDA ITEM NO. 13: **FUTURE BUSINESS**
13A: Antihyperlipidemic Review
13B: Antifungal Review
13C: Estrogen Replacement Products Review
13D: Neurontin™ Follow-Up Review
13E: Review of Elidel® and Protopic®
13F: Renal Product Review
13G: New Product Reviews
- **Symlin®**
- **Niravam®**

Materials included in agenda packet; submitted by Dr. Graham.
ACTION: NONE REQUIRED.

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

Doug Cox

From: FREELAND BROWN PHARMACY [fbpharm@freelandbrown.com]
Sent: Sunday, April 17, 2005 3:05 PM
To: Doug Cox
Subject: medicaid

I am a pharmacist who tries to work within the system to provide of our patients. This seems to be very difficult with the current guidelines that you have given the pharmacy community.

Why do we give condoms to people to prevent conception yet the ones that have made it to the living can NOT get the medications they need to stay alive?i.e. Caffeine citrate solution for children to help them not die in their sleep. Because it does not require a prescription to obtain the caffeine they are denied the drug. Mom and Dad can not go out buy if off the shelf and dilute to the proper concentration. That is our job. Also a person who has to have radiation treatments and gets a inflamed throat with other complications can not get dexamethasone, lidocain viscous, and Benadryl. Why, because of the OTC Benadryl. This seems a bit ridiculous to me. Other medications deemed unsuitable to fill would be like Questran in Aquaphor, since the Aquaphor is an OTC drug then that patient will have to live with a crying baby with a chapped buttocks, since all the other OTC medications for diaper rash did not help the child or the mother. Condoms are OTC and should not be dispensed by a pharmacy. If you want to then have them go to planned parenthood and get them free there. Your double standards seem quite obvious and not in the best interest of all people, infants as well as the terminal person who has the misfortune to be on Oklahoma Medicaid system.

Thank you for your time and consideration.
Dennis E. DuFour D. Ph.

DOUG COX, M.D.
State Representative
Delaware and Mayes Counties

Home:
33471 S. 595 Rd.
Grove, OK 74344
(918) 786-5381

Capitol:
State Capitol - Room 301
2300 N. Lincoln Blvd.
Oklahoma City, OK 73105-4885
(405) 557-7415
(800) 522-8502

House of Representatives

STATE OF OKLAHOMA
DISTRICT 5

VICE CHAIRMAN:
Health and Human Services

COMMITTEES:
Appropriations and Budget Sub Committee on Health and Social Services

Higher Education
Tourism and Recreation

April 20, 2005

Nico Gomez
Oklahoma Health Care Authority
4545 Lincoln, Suite 124
Oklahoma City, OK 73105

Dear Nico:

Enclosed you will find a copy of an email that I received with a Medicaid worry. This sounds like very legitimate concerns to me. Thought you might like to see it.

Sincerely,

Doug Cox

Rep. Doug Cox, M.D.

DC/jem
Enclosure
cc: Drug Utilization Review Board

MIKE FOGARTY
CHIEF EXECUTIVE OFFICER

Brad Henry
Governor

STATE OF OKLAHOMA

OKLAHOMA HEALTH CARE AUTHORITY

May 2, 2005

The Honorable Doug Cox
House of Representatives
301 State Capitol Building
Oklahoma City, OK 73105

Dear Representative Cox:

Thank you for forwarding the message from Dennis DuFour, pharmacist at Freeland Brown Pharmacy. Dr. DuFour expressed concern over the fact that non-prescription family planning products are available through the Medicaid pharmacy program while other pharmacy products are not covered by the program.

Family planning products are covered as a Medicaid benefit. Claims for these products may be filed using either a pharmacy claim or a professional services claim. The use of the pharmacy claim process for family planning products is intended to increase access to these products for Medicaid beneficiaries.

As you know, Medicaid is funded by both state and federal money. As such, programs under the Medicaid umbrella must comply with both state and federal law and regulations.

When considering the pharmacy program, federal requirements are set forth at 42 U.S.C. Section 1396r-8. In 1990, Congress enacted this legislation which requires that Medicaid programs receive the best price on pharmaceutical products by means of a rebate agreement. In return for the rebate, Medicaid agencies must provide coverage for drugs whose manufacturers agree to provide the rebate. The most significant factor determining coverage is the Federal Drug Rebate Agreement. Drugs for which no rebate agreement exists are not eligible for federal financial participation.

State law, codified at 56 O.S. Sec. 204, sets the requirements for the Oklahoma Medicaid pharmacy program, known as the Vendor Drug Program. Section 204(B) allows OHCA to require participation in the Federal Drug Rebate program as a condition of payment under the Vendor Drug Program. Section 204(C) requires OHCA to design the Vendor Drug Program in such as way as to earn "maximum federal financial participation."

Section 204(C) goes on to explicitly list 11 categories of drugs which may be excluded from the Vendor Drug Program. Non-prescription drugs are thereby considered an optional category for coverage under the Oklahoma Vendor Drug Program.

In order to comply with both state and federal regulations, the Vendor Drug Program is designed to provide coverage of drugs that (a) have a drug rebate agreement on file and (b) are not otherwise excluded from coverage. The Vendor Drug Program does provide coverage for some otherwise excludable drugs, such as Claritin OTC and Prilosec OTC. These two drugs, although both are non-prescription, participate in the Federal Drug Rebate Program and offer significant savings over their prescription version counterparts.

With this background in mind, let's take a look at the issues presented by Dr. DuFour.

1. Caffeine citrate solution – This drug is available as a non-prescription or prescription powder for compounding. Reimbursement hinges not only on the prescription status, but also the manufacturer's willingness to enter into a drug rebate agreement with the federal government. Many of the caffeine citrate powders are classified as over-the-counter medications, which puts them in the category of excludable drugs in both the state and federal statutes. Additionally, most of the manufacturer's do not have a rebate agreement in place, again running contrary to both state and federal law. This product is also available as a commercially prepared solution, and is reimbursable when the commercially prepared solution is billed.
2. The compounded product for throat pain can be mixed using another antihistamine product, such as hydroxyzine instead of OTC Benadryl, or can be mixed without an antihistamine. The two other products mentioned by Dr. DuFour are covered, and would be covered when mixed together, even though the FDA has not approved the combination. A pharmacist is reimbursed for compounded prescriptions by paying for each compensable ingredient in the compound plus a fee of $4.15.
3. Questran in Aquaphor has not been approved by the FDA for any use. Questran is used to lower cholesterol. Aquaphor is an ointment used in compounding topical preparations. As stated by the pharmacist, it is an OTC product and is not included in the wide range of products covered by the Medicaid pharmacy program. Several prescription preparations for diaper rash are covered.

We hope that this helps answer the questions raised by Dr. DuFour's email to you. If you have additional questions or would like further information, please do not hesitate to call me at (405) 522-7325.

Sincerely,

Nancy Nesser, J.D., D.Ph.
Pharmacy Director

The University of Oklahoma
Health Sciences Center
DEPARTMENT OF OBSTETRICS AND GYNECOLOGY
SECTION OF FEMALE PELVIC MEDICINE AND RECONSTRUCTIVE SURGERY/UROGYNECOLOGY

Dear Oklahoma DUR Committee Member,

I am writing to you as a practicing academic physician to voice my concern regarding recent discussions by Oklahoma Medicaid DUR Committee to prior authorize tolterodine extended release for urinary urge incontinence and overactive Bladder. The Oklahoma DUR Committee's possible recommendations to require the preferred agents oxybutynin and tolterodine immediate release to be used first is of a concern in my Medicaid patients that I treat every day.

Anticholenergic agents such as oxybutynin have been effective in treating my patients with urinary incontinence; however, in many patients the side effects have been too severe at therapeutic doses for the majority of them to tolerate. Dry mouth, dizziness, cognitive decrements, and constipation are side effects that increase medical utilization, morbidity and ultimately over all cost. The utilization of tolterodine immediate release in my Medicaid patients is a step forward in respect to oxybutynin treatment, but like all anticholenergic there is a dose response in terms of efficacy and side effects. Tolterodine extended release has demonstrated a superior balance pertaining to efficacy and tolerability in controlled clinical trials. The medical based evidence improvement is achieved with tolterodine extended release because of its pharmacology. Lower peak levels have corresponded to significantly fewer incidence of dry mouth and the higher trough levels correlates to significantly improvements in urge incontinence episodes.[1] Tolterodine extended release improved tolerability and efficacy will improve patient compliance as will its once a day dosing. Furthermore, a recent article on pharmacoecomics concludes that Tolerodine LA is cost effective in treating OAB. In the same reference Tolterodine immediate release formulation was not shown to be cost effective[4].

As incontinence, due to urge or in combination with stress incontinence (mixed incontinence), is primarily a female condition that affects my Medicaid urinary incontinent patients life every day and these daily incontinent episodes have shown double the risk of suicide attempts in medically ill patients.[2] The co-morbidity of psychological conditions like depression are certainly associated with urinary incontinence and a reduce quality of life[3]. Numerous clinical trials have concluded that women with mixed incontinence who undergo pelvic floor corrective surgery may not have an improvement in their condition until the urge component is addressed, putting patients at risk for possible unnecessary surgery and anesthesia.

I hope the committee will make tolterodine extended release capsules available for all Medicaid patients, because I have found that my patient population, and medical based evidence medicine supports its use for urinary urge incontinence and other overactive bladder symptoms. When the over all cost is considered, I have found tolterodine extended release to be the most cost effective conservative approach to medical management in women with urge or mixed incontinence.

Respectfully,

S Shobeiri

Dr. SIA Shobeiri, M.D.
OUHSC Director of Female Pelvic Medicine and Reconstructive Surgery

1. J. of Urology: 2001; 57(3), p.414-21
2. Arch IM: 2004; 164, p. 79-84
3. Am J Obster Gynecol: 2002, p.80-87
4. Pharmacoeconomics; 2004: 22(16), p.1047-59

APPENDIX B

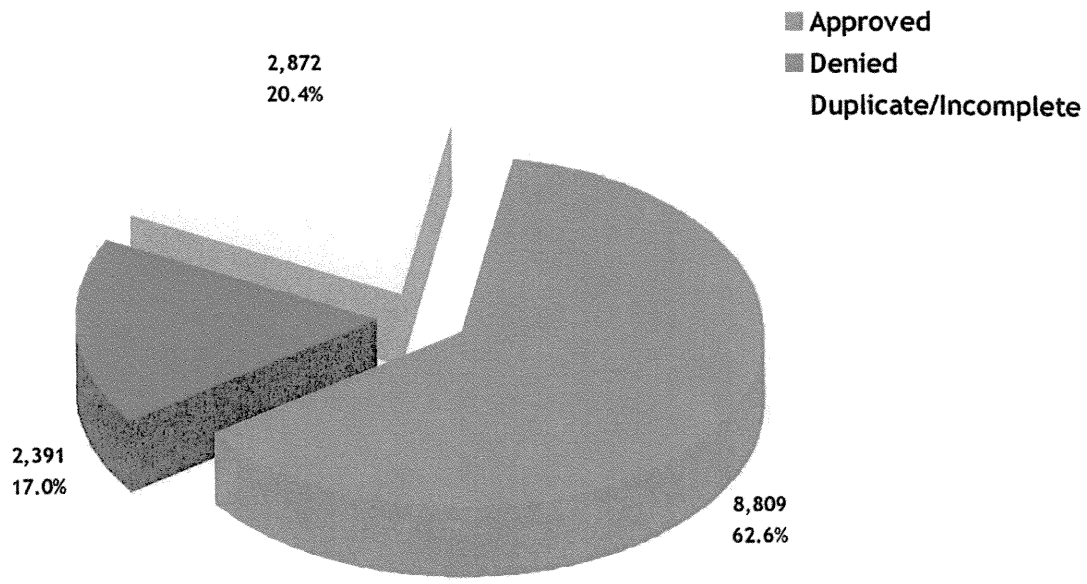
Retrospective Drug Utilization Review Report

Claims Reviewed for February 2005

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Total # of messages returned by system when no limits were applied	99,461	98,054	849,490	52,561
Limits which were applied	Established, major, males 65 yrs old & older	Acetaminophen, males 65 yrs old & older	Contraindicated, females aged 50-69 yrs, non-nursing home, with heart failure	Statins, high dose
Total # of messages after limits were applied	181	84	438	43
Total # of clients reviewed after limits were applied	181	75	426	43

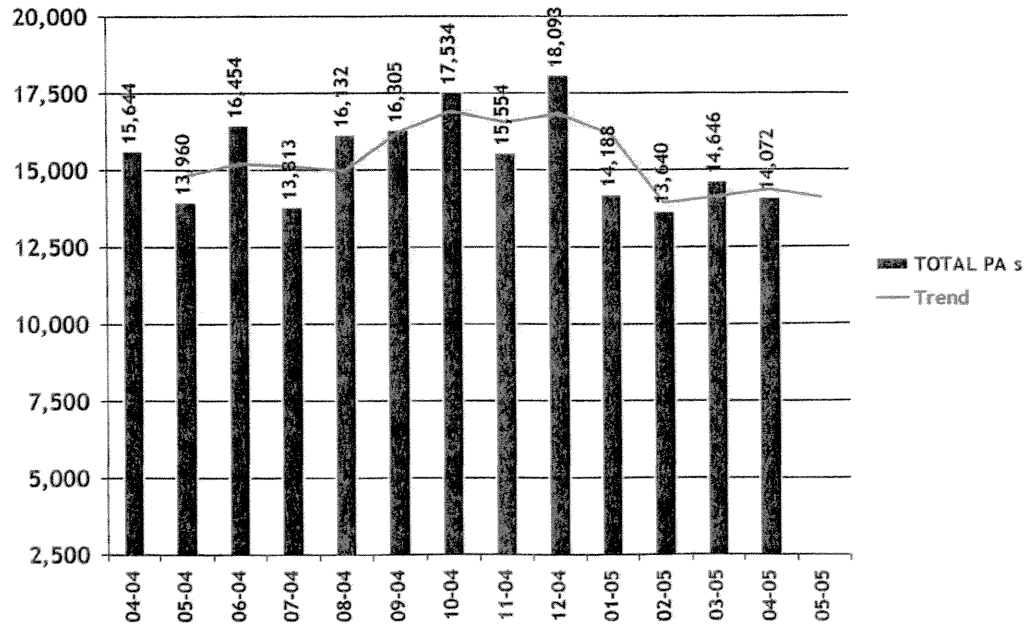
LETTERS			
Prescribers		**Pharmacies**	
Sent	**Responded**	**Sent**	**Responded**
119		21	

PRIOR AUTHORIZATION ACTIVITY REPORT
April 2005



PHARMACY Management Consultants

PRIOR AUTHORIZATION REPORT
April 2004 - April 2005



PHARMACY Management Consultants

Date Processed: Tuesday, May 03, 2005

Activity Audit for

April 01 2005 Through April 30 2005

Date	Antiulcers app.	Antiulcers den.	Anxiolytic/ Hypnotics app.	Anxiolytic/ Hypnotics den.	Antihistamine app.	Antihistamine den.	Growth Hormones app.	Growth Hormones den.	Stimulant app.	Stimulant den.	Nsaids app.	Nsaids den.	ACE Inhibitors app.	ACE Inhibitors den.	HTN Combos app.	HTN Combos den.	Calcium Channel Blockers app.	Calcium Channel Blockers den.	Plavix app.	Plavix den.	ARB app.	ARB den.	Anti-depressants app.	Anti-depressants den.	Daily Total
App.	18		4063		1273		23		947		147		49		7		96		793		21		137		
Den.		5		453		706		5		198		145		57		3		182		97		10		61	
Average Length of Approvals in Days	27		107		97		168		218		322		188		158		320		349		279		100		

Changes to existing PA's	1023
Total (Previous Year)	15644

* Denial Codes	
762 = Lack of clinical information	7.19%
763 = Medication not eligible	2.13%
764 = Existing PA	5.86%
772 = Not qualified for requested Tier	5.02%
773 = Requested override not approved	12.88%

SUPER PA's	
Admitted to Nursing Home	109
Early Refill Attempts	53821
Dosing Change	661
Lost/Broken Rx	139
Stolen	34
Other	86
Wrong D.S. on Previous Rx	92
Quantity vs. Days Supply	326
Brand	285
-- Approved	107
-- Denied	92

Monthly Totals	Number	Percent of Total
Approved	8764	62.28%
Additional PA's	43	0.31%
Emergency PA's	2	0.01%
Duplicates	659	4.68%
Incompletes	2213	15.73%
Denied *	2391	16.99%
Total	14072	100.00%

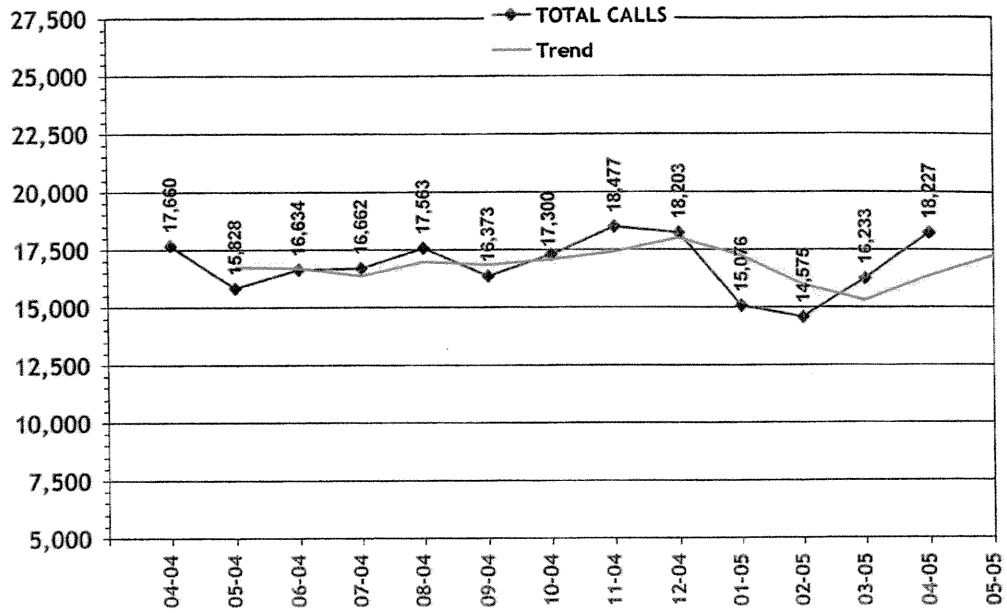
Daily Average of 541.23 for 26 Days

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.)

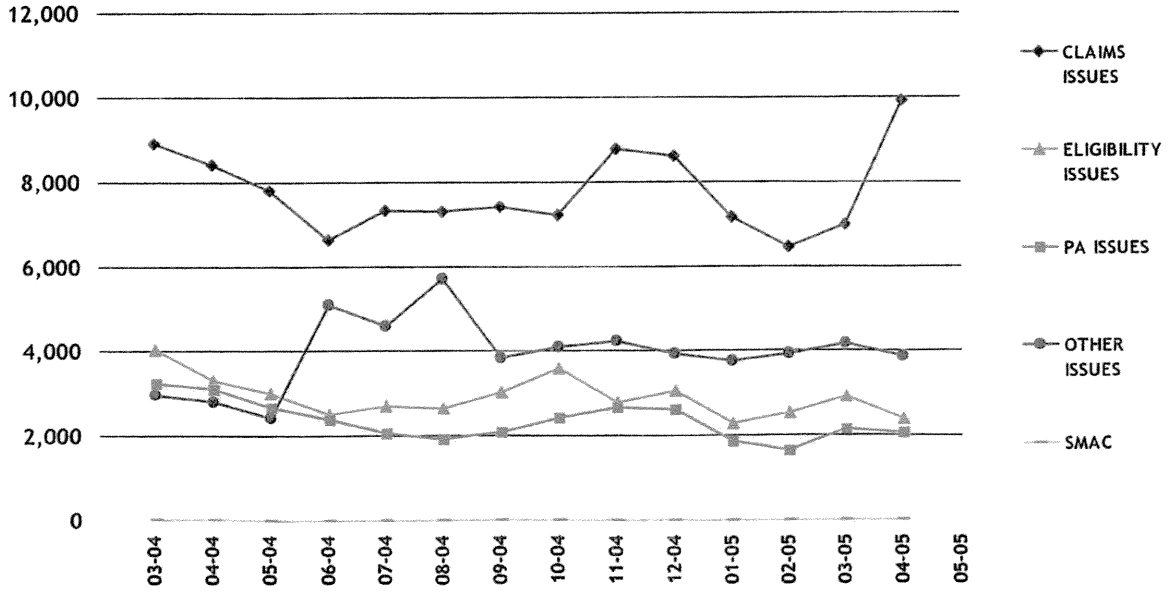
CALL VOLUME MONTHLY REPORT
April 2004 - April 2005



PHARMACY Management Consultants

CALL VOLUME ISSUES

April 2004 - April 2005



PHARMACY Management Consultants

APPENDIX C

Vote to Prior Authorize Antidepressants
Oklahoma Medicaid
March 2005

Recommendations

The college of pharmacy recommends placing the suggested dual-acting anti-depressants on tier-2 pending results of long-term clinical trials assessing the long-term efficacy and safety as compared to the older anti-depressants.

1. Approval of tier-2 medication after a recent 4 week trial on a tier one medication. Tier-1 selection can be from any tier-1 anti-depressant classification.
2. Approval of tier-2 medication if there is a documented adverse effect, drug interaction, or contraindication to tier-1 products.
3. Approval of tier-2 medication if there is prior stabilization on the tier-2 medication documented within the last 100 days.
4. Approval of tier-2 medication if there is a unique FDA-approved indication not covered by any tier-1 products.
5. A petition for a tier-2 medication may be submitted for consideration when a unique client specific situation exists.

Antidepressants*	
Tier-1	*Tier-2*
Dual Acting Antidepressants	
Mirtazapine (Remeron®)	Duloxetine (Cymbalta®)
Mirtazapine (Remeron Soltab®)	Venlafaxine (Effexor, Effexor XR®)
Trazodone (Desyrel®)	Bupropion (Wellbutrin XL®)
Bupropion (Wellbutrin, Wellbutrin SR®)	Nefazodone (Serzone®)**
Selective Serotonin Re-Uptake Inhibitors* **	
Fluoxetine (Prozac®)	Fluoxetine (Sarafem®) Fluoxetine Tablets and 40 mg Capsules
Fluvoxamine (Luvox®)	
Paroxetine (Paxil®)	
Paroxetine (Paxil CR®)	
Paroxetine mesylate (Pexeva®)	
Sertraline (Zoloft®)	
Citalopram (Celexa®)	Citalopram (Celexa®) Liquid
Escitalopram (Lexapro®)	Escitalopram (Lexapro®) Liquid
Secondary Amine Tricyclics	
Desipramine (Norpramin®)	
Nortriptyline (Pamelor®)	
Protriptyline (Vivactil®)	
Tertiary Amine Tricyclics	
Amitriptyline (Elavil®)	
Clomipramine (Anafranil®)	
Doxepine (Sinequan®)	
Imipramine (Tofranil-PM®)	
Trimipramine (Surmontil®)	
Tetracyclics	
Amoxapine (Asendin®)	
Maprotiline (Ludiomil®)	
Monoamine Oxidase Inhibitors	
	Phenelzine (Nardil®)
	Tranylcypromine (Parnate®)

* Brand-Name Override required where applicable.

** Bristol-Myer Squibb has discontinued marketing of brand name Serzone® due to possible link to hepatic toxicity.

*** Current SSRI tiers based on Supplemental Rebate participation.

APPENDIX D

30 Day Notice of Intent to Prior Authorize Zelnorm®

Oklahoma Medicaid
May 2005

Manufacturer Novartis

Classification FDA classification: 5-HT_4 receptor partial agonist
Status: prescription only

Summary Tegaserod is a 5-HT_4 receptor partial agonist indicated for the treatment of IBS with constipation in women and chronic idiopathic constipation in patients under 65 years of age.

Recommendations

The College of Pharmacy recommends prior authorization be placed on Zelnorm® with the following criteria:

- Constipation-Predominate IBS in <u>women</u> that meet the following criteria:
  - At least one of the following present - Abdominal pain/discomfort, which is:
    - Relieved with defecation
    - And/or associated with change in stool frequency
    - And/or associated with changes in stool consistency
  - Two or more of the following (equal or greater than 2 days per week)
    - Altered stool frequency (greater than 3 bowel movements per day)
    - Altered stool form (lumpy/hard or loose/watery)
    - Passage of mucus
    - Bloating or feeling abdominal distension
- Chronic Idiopathic Constipation in males and females who meet the following criteria:
  - Patient is between 19 and 65 years of age
  - Have documentation that constipating therapies for other disease states have been discontinued
  - Documented and updated Colon Screening (>50 years of age)
- For both diagnoses, hydration and treatment attempts with a minimum of three alternate products must be documented.
- Initial approval for 12 weeks of therapy. An additional year approval may be granted if physician documents client is responding well to treatment.

Economic Impact

Utilization

January 2004 through December 2004

Clients	Cost	Claims	Units	Days	Cost/ Unit	Cost/ Claim	Cost/ Day	Cost/ Client
1,197	$ 549,406.27	3,591	214,612	110,887	$ 2.56	$ 152.99	$ 4.95	$ 458.99

	Calendar Year 2003	*Calendar Year 2004*	*Percent Change*	
Total Clients	522	1,197	Increased	129.3 %
Total Claims	1,254	3,591	Increased	186.4 %
Total Cost	$ 169,847.53	$ 549,406.27	Increased	223.5 %
Total Days	38,069	214,612	Increased	463.7 %
Per Diem	$ 4.46	$ 4.95	Increased	11.0 %

CY04

Age	Female	Male	Totals
0 to 9	6	6	45
10 to 19	83	14	97
20 to 34	155	15	170
35 to 49	267	28	295
50 to 64	238	33	271
65 to 79	195	31	226
80 to 94	109	8	117
95 and Over	9	0	9
Totals	**1,062**	**135**	**1,197**

Annual Savings Estimates

Potential savings based on CY04 utilization.

Use Reduction	PA Cost[1]	Clients Approved	Projected Reimbursement	Projected Savings[2]
↓25%	$ 27,172.15	898	$ 412,169.45	$ 110,064.67
↓33%	$ 25,914.06	801	$ 367,647.80	$ 155,844.41
↓50%	$ 20,940.07	418	$ 191,626.66	$ 336,839.54
↓75%	$ 19,403.12	299	$ 137,236.82	$ 392,766.33

[1]The average cost for processing petitions is calculated at $6.75 per petition with the maximum cost at $12.97 per petition. The maximum cost was used in the estimation of administrative costs. PA Cost = 1 PA request for all clients effected plus 1 additional PA request per each approved client.

[2]Projected Savings = (Current Reimbursement - Projected Reimbursement) - PA Cost. Cost reductions were not taken for rebates or dispensing fees.

APPENDIX E

30 Day Notice of Intent to Prior Authorize Niravam® (alprazolam)

Oklahoma Medicaid
May 2005

Manufacturer Schwarz

Classification FDA classification: Schedule IV, benzodiazepine
Status: prescription only

Summary

Niravam® is an orally disintegrating form of alprazolam. It is indicated for the treatment of anxiety (up to 4mg/day) and panic disorder (up to 10mg/day).

Recommendations

The College of Pharmacy recommends Prior Authorization of Niravam® which could be approved with an FDA approved diagnosis for the use of Niravam®, a diagnosis indicating that the client has a condition that prevents them from swallowing tablets, and the physician's signature.

Dosing regimens that involve splitting of tablets will not be covered.

Cost comparison

	Estimated Acquisition Cost (EAC) / Unit	Daily Dose	Monthly Dose (30 day supply – 1 to 4 times daily)	SMAC Cost for alprazolam tablets (30 day supply – 1 to 4 times daily)
Niravam® 0.25mg	$ 1.09	Up to 10mg	$ 32.70 - $ 130.80	$ 1.50 - $ 6.00
Niravam® 0.50mg	$ 1.35	Up to 10mg	$ 40.50 - $ 162.00	$ 2.40 - $ 9.60
Niravam® 1mg	$ 1.81	Up to 10mg	$ 54.30 - $ 217.20	$ 2.70 - $ 10.80
Niravam® 2mg	$ 3.07	Up to 10mg	$ 92.10 - $ 460.50*	$ 5.40 - $ 27.00*

*Maximum cost based on a 10 mg daily dose.

APPENDIX F

30 Day Notice of Intent to Prior Authorize Symlin® (pramlintide acetate)

Oklahoma Medicaid
May 2005

Manufacturer Amylin Pharmaceuticals, Inc

Classification FDA classification: Antihyperglycemic
Status: Prescription only

Summary

Symlin® is an injectable antihyperglycemic drug for use in type 1 and type 2 diabetic patients, as adjunctive treatment in patients who use mealtime insulin therapy and who have failed to achieve desired glucose control despite optimal insulin therapy. It is a synthetic analog of human Amylin, a naturally occurring hormone synthesized by pancreatic beta cells that contributes to glucose control during the postprandial period.[1]

Recommendations

The College of Pharmacy recommends the following:

- Require prior authorization for Symlin®
- Patients must meet FDA approved selection criteria:

Patients with type 1 and 2 diabetes using insulin must:

1. have failed to achieve adequate glycemic control;
2. are receiving ongoing care under the guidance of a health care professional

Patients meeting the following criteria should **NOT** be considered for Symlin® therapy:

1. poor compliance with insulin regimen
2. poor compliance with self-blood glucose monitoring
3. HbA1c> 9%
4. recurrent severe hypoglycemia requiring assistance in past 6 months
5. presence of hypoglycemia unawareness
6. diagnosis of gastroparesis
7. require use of drugs that stimulate GI motility
8. pediatric patients

	Average Wholesaler Price (AWP) / ML	Daily Dose	Monthly Dose (30 day supply at 3 doses daily)
Symlin®	$19.88	30mcg to 120 mcg at each meal	$ 99.40 to $ 397.60

Pharmacological data

Amylin is co-located with insulin in secretory granules and co-secreted with insulin by the pancreatic beta cells in response to food intake. In healthy individuals, Amylin and insulin show similar fasting and postprandial patterns. Amylin affects the rate of postprandial glucose appearance through a variety of mechanisms. Amylin slows gastric emptying (i.e., the rate at which food is released from the stomach to the small intestine) without altering the overall absorption of nutrients. In addition, Amylin suppresses glucagon secretion (not normalized by insulin alone), which leads to suppression of endogenous glucose output from the liver. Amylin also regulates food intake due to centrally-mediated modulation of appetite. In patients with insulin-using type 2 or type 1 diabetes, the pancreatic beta cells are dysfunctional or damaged, resulting in reduced secretion of both insulin and amylin in response to food. [1]

Therapeutic indications

- Type 1 diabetes, as an adjunct treatment in patients who use mealtime insulin therapy and who have failed to achieve desired glucose control despite optimal insulin therapy.

- Type 2 diabetes, as adjunct treatment in patients who use mealtime insulin therapy and who have failed to achieve desired glucose control despite optimal insulin therapy.

Bioavailability/pharmacokinetics

Absorption

- Absolute bioavailability of a single dose ~ 30-40%
- Subcutaneous (SC) administration of different doses into the abdominal area or thigh resulted in dose-proportionate maximum concentrations (C_{max}) and overall exposure (AUC) (Table 1[1]).

Table 1: Mean Pharmacokinetic Parameters Following Administration of Single SC Doses of Symlin®

SC Dose (µg)	AUC (0-8) (pmol*min/L	Cmax (pmol/L)	Tmax (min)	Elimination t (min)
30	3750	39	21	55
60	6778	79	20	49
90	8507	102	19	51
120	11970	147	21	48

Distribution

- Symlin® does not extensively bind to blood cells or albumin (~ 40% of drug is unbound in plasma)

Metabolism and Elimination

- The half life is ~ 48minutes. Symlin® is metabolized primarily by the kidneys. Primary metabolite (Des-lys[1] pramlintide (2-37 pramlintide) has a similar $t_{1/2}$ AUC values are relatively constant with repeat dosing, indicating no bioaccumulation.

Dosage forms

Injectable

- Available as 5ml vials containing 0.6ml pramlintide (as acetate).

Dosage range

- **Type 1 Diabetes**- Initiate at 15µg and titrate at 15µg increments. Maintenance dose- 30 µg or 60 µg.
- **Type 2 Diabetes**- Initiate at 60 µg and increase to 120 µg as tolerated.

Known adverse effects/toxicities

Severe hypoglycemia (black box warning), Nausea, Anorexia, Vomiting, Abdominal pain, Headache, Fatigue, Dizziness, Coughing, Pharyngitis, Allergic reaction, Local injection site reaction.

Special precautions

- **Hypoglycemia**
- **Symlin® and insulin should always be administered as separate injections and never be mixed**
- **Renal and hepatic impairment**- no studies have been done on these patients. Currently the dosing requirement does not need to be altered in these patients.
- **Local allergy** – Patients may experience redness, swelling or itching at the injection site. These usually resolve within a few days to a few weeks

Contraindications

- Hypersensitivity to any of the ingredients
- Gastroparesis
- Hypoglycemia unawareness

Drug interactions

- Anticholinergic agents
- a-glucosidase inhibitors
- Agents that slow GI motility or GI absorption
- Oral medications with rapid onset (administer these agents at least 1 hour prior or 2 hours after Symlin® injection
- Insulin (not to be mixed and must be administered separately

Patient Selection

Proper patient selection is critical to safe and effective use of SYMLIN®. Before initiation of therapy, the patient's HbA1c, recent blood glucose monitoring data, history of insulin-induced hypoglycemia, current insulin regimen, and body weight should be reviewed. SYMLIN® therapy should only be considered in patients with insulin-using type 1 or 2 diabetes who fulfill the following criteria:

- have failed to achieve adequate glycemic control despite individualized insulin management;
- are receiving ongoing care under the guidance of a health care professional skilled in the use of insulin and supported by the services of diabetes educator(s).

Patients meeting any of the following criteria should **NOT** be considered for SYMLIN® therapy:

- poor compliance with current insulin regimen;
- poor compliance with prescribed self-blood glucose monitoring;
- have an HbA1c >9%;
- recurrent severe hypoglycemia requiring assistance during the past 6 months;
- presence of hypoglycemia unawareness;
- confirmed diagnosis of gastroparesis;
- require the use of drugs that stimulate gastrointestinal motility;
- pediatric patients.

REFERENCES

1. Symlin® package insert

APPENDIX G

Drug Utilization Review of Antihyperlipidemics

Oklahoma Medicaid

May 2005

Hyperlipidemia and Currently Available Treatment Options

Hyperlipidemia has been demonstrated to be a major risk factor for developing cardiovascular diseases. Currently, lipid lowering therapy has become an important factor in the treatment of cardiovascular disease due to the emerging randomized clinical trials showing reduction of lipid parameters significantly reduced the incidence of cardiovascular events. The following table shows the various types of hyperlipidemias.

Hyperlipidemia Classification[1, 2]
(Fredrickson Classification)

Type	*Hyperlipidemia Name*	*Lipoprotein Class Elevated*	*Lipid Elevation*		*Approved Drug Therapy*	*Genetic Disorder*
			Major	*Minor*		
	Hyperlipemia, exogenous	Chylomicrons	TG	C‡	none	Familial lipoprotein lipase deficiency, Familial apolipoprotein C-II deficiency
IIa	Hyper-cholesterolemia	LDL	C		Atorvastatin, Cholestyramine Colesevelam, Colestipol Dextrothyroxine, Ezetimibe Fluvastatin, Lovastatin, Niacin Pravastatin, Probucol, Simvastatin	Familial hypercholesterolemia, Familial combined hyperlipidemia, Polygenic hypercholesterolemia
IIb	Hyperlipidemia, combined	LDL, VLDL	C	TG	Atorvastatin, Cholestyramine Clofibrate, Colesevelam, Colestipol Fluvastatin, Gemfibrozil, Lovastatin Niacin, Pravastatin, Probucol, Simvastatin	Familial combined hyperlipidemia
III	Hyperlipidemia, remnant	IDL	C/TG		Atorvastatin, Clofibrate, Gemfibrozil, Niacin, Pravastatin, Simvastatin	Familial dysbetalipoproteinemia
IV	Hyperlipemia, endogenous	VLDL	TG	C‡	Atorvastatin, Clofibrate, Fenofibrate, Gemfibrozil, Niacin, Pravastatin, Simvastatin	Familial hypertriglyceridemia (mild) Familial combined hyperlipidemia Sporadic hypertriglyceridemia Tangier disease
V	Hyperlipemia, mixed	Chylomicrons VLDL	TG	C‡	Clofibrate, Fenofibrate, Gemfibrozil Niacin	Familial hypertriglyceridemia (severe) Familial lipoprotein lipase deficiency Familial apolipoprotein C-II deficiency

‡ Increases or no change; *C*=cholesterol; *TG*=triglycerides; *LDL*=low-density lipoprotein; *VLDL*=very-low-density lipoprotein; *IDL*=intermediate-density lipoprotein

Below are the recommended values as established by the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of hyperlipidemias:

	LDL (mg/dL)	Triglycerides (mg/dL)	HDL (mg/dL)
Desired	*< 100*	*< 150*	*> 60*
Borderline High	*100 - 129*	*150 - 199*	
High	*130 - 159*	*200 - 499*	
Very High	*> 160*	*> 500*	

As medical research increases the understanding of the benefits associated with cardiovascular disease outcomes, lipid lowering therapies are emerging and expanding to add new agents with different mechanisms of action. Omacor®, a purified form of omega-3 acid ethyl ester extracted from marine fish,

has been approved by the FDA as an adjunct along with diet and exercise for the treatment of extremely elevated TG (>500 mg/dL.) Currently, the following agents are available for treatment of hyperlipidemia:

Pharmacologic Class	LDL-C	Triglycerides	HDL-C
Bile Acid Sequestrants	↓ 10-30%	↑ 3-10%	Unchanged
Fibric Acid Derivatives	↓ 5-10%*	↓ 30-60%	↑ 5-10%
Nicotinic Acid Derivatives	↓ 10-25%	↓ 5-30%	↑ 15-25%
HMG-CoA Reductase Inhibitors	↓ 20-55%	↓ 10-30%	↑ 5-15%
Cholesterol Absorption Inhibitor	↓ 15-18%	↓ 7-9%	↑ 1%

*Fenofibrate may increase LDL-C levels

Bile Acid Sequestrants

- Lowers plasma cholesterol by binding bile acids in the intestines, thereby inhibiting their reabsorption and enterohepatic cycling, and increases their fecal excretion. Interruption of enterohepatic bile acid recirculation results in reduction of intrahepatic cholesterol stores. The decrease in intrahepatic cholesterol increases the number of LDL receptors in the liver, enhancing the clearance of LDL-cholesterol from the circulation.
- May be used as sole agent for treatment of moderate elevation of LDL cholesterol in young adults or in women who may be considering pregnancy.
- May be useful as adjunctive treatment when used in combination with statins for treatment of very high LDL cholesterol.
- Possess little to no systemic side effects due to local action in the small intestines. However, BAS do affect absorption of fat soluble vitamins and may increase bleeding tendencies due to decrease in Vitamin K absorption.

Fibric Acid Derivatives

- Increases lipoprotein lipase activity, which is the enzyme that catalyzes lipolysis of the triglyceride core of the chylomicron and catabolism of VLDL, thus lowering TG levels.
- Recommended in patients with very high TG to reduce the risk for acute pancreatitis or in patients with elevated TG.
- May be used as an adjunctive treatment with statins for patients with both elevated LDL and atherogenic dyslipidemia.
- The most common adverse effects of fibric acid derivatives are gastrointestinal distress, skin reactions, myopathy, and cholesterol gallstones. Take with food.
- There are currently four fibric acid derivatives. However, bezafibrate is not available in the United States, and clofibrate is available but rarely used.

Drug	Brand Name	Usual Adult Dose	Available Dosage Forms	FDA Indications
Clofibrate	Atromid-S®	500 mg QID	Capsule: 500 mg	Hypercholesterolemia Central Diabetes Insipidus
Fenofibrate	TriCor® Lofibra® Antara®	54-160 mg QD 67-200 mg QD 43-130 mg QD	Tablet: 54, 160 mg Capsule: 67, 134, 200 mg Capsule: 43, 87, 130 mg	Hypercholesterolemia, Hypertriglyceridemia
Gemfibrozil	Lopid®	600 mg BID	Tablet: 600 mg	Hypercholesterolemia, Reduction of CHD risk

- TriCor® has recently received FDA approval for a new formulation that utilizes nanoparticle technology to allow the drug to dissolve faster and more completely in the gastrointestinal tract. This allows the medication to be taken with or without food. The Lofibra and Antara are also micronized fenofibrate formulations. Although all the products result in the same degree of lipid lowering outcome, they are not interchangeable as each holds a patent for its own micronization process.

Nicotinic Acid Derivatives

- Several possible modes of action have been proposed including, inhibition of hepatic synthesis of lipoproteins containing apolipoprotein B-100, promotion of lipoprotein lipase activity, and reduction of free fatty acid mobilization from adipose tissue with an increase in fecal output of sterols.
- Its current place in therapy lies in its ability to lower TG levels and raise HDL levels.
- May be used as sole agent in patients near goal or as an adjunctive treatment with a statin.
- Common side effects include facial flushing, upset stomach, and pruritus.

Cholesterol Absorption Inhibitor (Zetia®)

- Inhibits passage of dietary and biliary cholesterol across the brush border of the small intestine, with minimal or no effect on absorption of other soluble food nutrients.
- May be used as a sole agent in patients with moderate hyperlipidemia.
- May be used as adjunctive treatment with a statin to increase the level of LDL reduction in patients who are not already at goal on a statin.
- Common side effects are upset stomach, diarrhea, joint pain, fatigue, and headache.
- Cholesterol absorption inhibitors are currently marketed as alternatives to statins or as an add-on agent for clients who are not at goal with a statin.

Utilization of Antihyperlipidemia Therapies

During the 2004 fiscal year, 22,677 clients utilized antihyperlipidemic agents resulting in 102,593 claims and a total cost of $13,596,503.73.

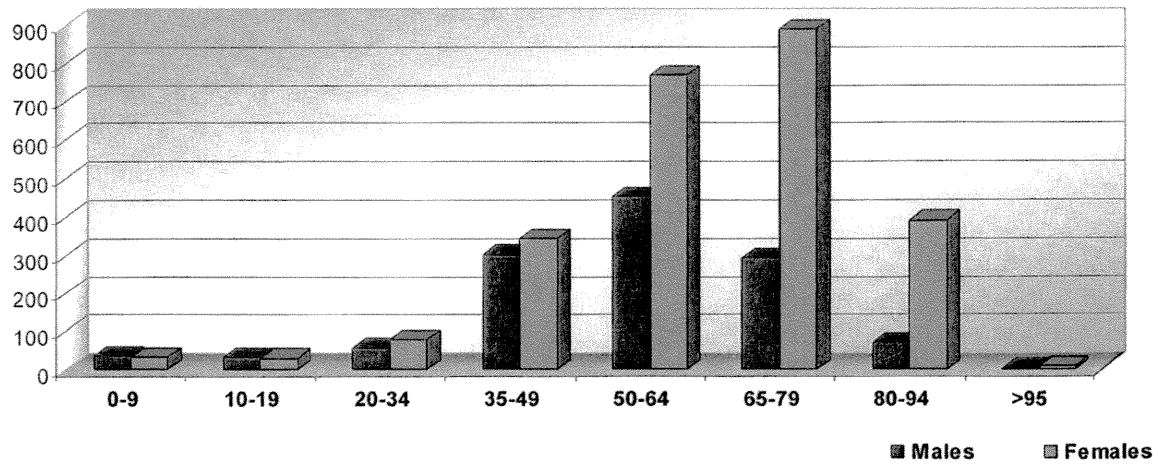
Trends in Utilization of Antihyperlipidemia Therapies

	Fiscal Year 2003	*Fiscal Year 2004*	*Percent Change*	
Total Claims	**87,386**	**102,593**	**Increased**	**17.4 %**
Bile Acid Sequestrants	2,337	2,335	Decreased	0.09 %
Fibric Acid Derivatives	7,532	9,120	Increased	21.1 %
Nicotinic Acid Derivatives	915	968	Increased	5.79 %
HMG-CoA Reductase Inhibitors	76,602	87,778	Increased	14.6 %
Cholesterol Absorption Inhibitor	N/A	2,392		N/A
Total Cost	**$ 10,466,968.04**	**$ 13,596,503.73**	**Increased**	**29.9 %**
Bile Acid Sequestrants	$ 156,096.36	$ 163,083.34	Increased	4.48 %
Fibric Acid Derivatives	$ 371,829.67	$ 543,999.52	Increased	46.3 %
Nicotinic Acid Derivatives	$ 51,970.72	$ 73,283.10	Increased	41.0 %
HMG-CoA Reductase Inhibitors	$ 9,887,071.29	$ 12,545,282.28	Increased	26.9 %
Cholesterol Absorption Inhibitor	$ N/A	$ 270,854.49		N/A
Avg Cost per-Diem	**$ 2.07**	**$ 2.28**	**Increased**	**10.0 %**
Bile Acid Sequestrants	$ 2.57	$ 2.65	Increased	3.11 %
Fibric Acid Derivatives	$ 1.29	$ 1.49	Increased	15.5 %
Nicotinic Acid Derivatives	$ 1.42	$ 1.77	Increased	24.6 %
HMG-CoA Reductase Inhibitors	$ 2.98	$ 3.13	Increased	5.03 %
Cholesterol Absorption Inhibitor	$ N/A	$ 2.37		N/A

Details of Antihyperlipidemia Drug Utilization
(Not including Statins)

Drug	Clients	Claims	Units	Days	Costs	PerDiem
CHOLESTYR POW 4GM CAN	220	516	200,998	10,393	$25,314.19	$2.44
CHOLESTYR POW 4GM PKTS	226	509	29,837	14,610	$35,280.17	$2.41
CHOLESTYR POW 4GM LITE CAN	104	215	59,617	4,604	$9,065.97	$1.97
CHOLESTYR POW 4GM LITE PKTS	76	155	11,642	4,559	$12,713.58	$2.79
COLESTID GRA 5GM	5	5	1,980	143	$414.96	$2.90
COLESTID POW 5GM	21	83	5,360	2,436	$9,367.16	$3.85
COLESTID TAB 1GM	135	360	30,612	10,846	$17,201.62	$1.59
COLESTID FLA GRA 5/7.5GM	2	10	480	480	$1,001.34	$2.09
COLESTID FLA GRA 5GM	2	9	4,050	250	$741.10	$2.96
PREVALITE POW 4GM CAN	13	28	7,812	484	$1,318.10	$2.72
PREVALITE POW 4GM PKTS	21	37	2,082	1023	$2,327.32	$2.27
QUESTRAN POW 4GM CAN	15	28	11,264	714	$1,994.12	$2.79
QUESTRAN POW 4GM PKTS	13	14	734	423	$1,039.93	$2.46
QUESTRAN POW 4GM LITE CAN	5	10	2,948	150	$514.97	$3.43
QUESTRAN POW 4GM LITE PKTS	1	1	240	15	$308.56	$20.57
WELCHOL TAB 625MG	86	355	55,038	10,346	$44,480.25	$4.30
All Bile Acid Sequestrants	**827**	**2,335**	**424,694**	**61,476**	**$163,083.34**	**$2.65**
FENOFIBRATE CAP 200MG	2	3	150	150	$297.46	$1.98
LOFIBRA CAP 67MG	1	1	60	60	$47.26	$0.79
LOFIBRA CAP 134MG	5	10	347	347	$501.76	$1.45
LOFIBRA CAP 200MG	3	14	412	412	$931.39	$2.26
TRICOR TAB 54MG	177	677	33,886	28,911	$34,456.82	$1.19
TRICOR TAB 160MG	673	2,538	130,734	127,203	$381,551.21	$3.00
TRICOR CAP 200MG	1	1	90	90	$206.84	$2.30
GEMFIBROZIL TAB 600MG	1334	5,854	392,812	206,003	$124,959.16	$0.61
LOPID TAB 600MG	12	22	1,630	970	$1,047.62	$1.08
All Fibric Acid Derivatives	**2,133**	**9,120**	**560,121**	**364,146**	**$543,999.50**	**$1.49**
Niaspan TAB 500mg ER	246	738	45,397	31,177	$49,278.50	$1.58
Niaspan TAB 750mg ER	10	42	2,638	1,551	$4,028.00	$2.60
Niaspan TAB 1000mg ER	57	188	10,640	8,749	$19,976.60	$2.28
All Nicotinic Acid Derivatives	**294**	**968**	**58,675**	**41,477**	**$73,283.10**	**$1.77**
Zetia TAB 10mg	737	2,392	116,204	114,473	$270,854.49	$2.37
Cholesterol Absorption Inhibitor	**737**	**2,392**	**116,204**	**114,473**	**$270,854.49**	**$2.37**
Total	3,772	14,815	1,159,694	581,572	$1,051,220.40	$1.80

Demographics of Clients Utilizing Antihyperlipidemia Therapies
(Not including Statins)



Conclusion and Recommendation

The College of Pharmacy recommends a preferred drug list for the Fibric Acid Derivatives as follows:

Fibric Acid Derivatives	
Tier One	***Tier Two***
Lofibra® 67mg Caps	Tricor® 48mg Tabs
Lofibra® 134mg Caps	Tricor® 145mg Tabs
Lofibra® 200mg Caps	Antara® 43mg Caps
Gemfibrozil 600mg Tabs	Antara® 130mg Caps
Clofibrate 500mg Caps	

The College of Pharmacy also recommends a prior authorization be placed on Zetia®. The approval criterion is as follows:

1. Diagnosis:
   - Hypercholesterolemia, primary
   - Hypercholesterolemia, homozygous familial
   - Sitosterolemia, homozygous

2. Laboratory documentation that client has not met (LDL) cholesterol goals after therapeutic lifestyle changes and statin therapy for at least 6 months.

3. Not a candidate for statin therapy due to:
   - Documented active liver disease.
   - Documented unexplained, persistent elevations of serum transaminases.
   - Documented statin related myopathy.

The College of Pharmacy will conduct the annual review of the Statin Product Based Prior Authorization Category later this year.

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[1] Dorland's Illustrated Medical Dictionary 29th edition. W.B. Saunders, Philadelphia, 2003; 853.

[2] Website: US Food and Drug Administration. Online. Internet. 2003. Available: http://www.fda.gov/cder

[3] MICROMEDEX(R) Healthcare Series Vol. 124 expires 6/2005.

[4] Grundy SM. Physician s' Desk Reference Clinical Handbook: Hyperlipidemia. © 2003 Montvale, NJ.

APPENDIX H

Pharmacoeconomic Review of Elidel® (Pimecrolimus) and Protopic® (Tacrolimus)

Oklahoma Medicaid
May 2005

Pharmacological data

The active ingredient in Protopic® is tacrolimus and Elidel® is pimecrolimus. Both are microbial-derived macrolides with a mechanism of action similar to cyclosporine. They are believed to decrease both cytokine production and release of inflammatory mediators due to cell-mediated immune responses. The inhibitory binding consequently leads to reduced t-lymphocyte activation and immunosuppression. The characteristic high molecular weight and lipophilicity of these agents reduces systemic absorption but consideration of body surface area (BSA) and severity of disease plays a vital role in systemic absorption. In addition, the BSA and weight ratio should be assessed when treating children to minimize systemic effects.

The concentration of medication is usually confined to cutaneous surface of skin. The systemic permeation of medication is determined by severity of dermatitis. As the skin barriers improves the subsequent systemic absorption decreases.

Therapeutic indications

- *Elidel® (Pimecrolimus)*-Short-term to intermittent treatment of mild to moderate atopic dermatitis (eczema) in non-immunocompromised patients over 2 years of age whom are not responsive or intolerant to conventional treatments.
- *Protopic® (Tacrolimus)*- Short-term to intermittent treatment of moderate to severe atopic dermatitis (eczema) in non-immunocompromised patients over 2 years of age whom are not responsive or intolerant to conventional treatments.

Dosage forms

Topical

- Protopic® (Tacrolimus) 0.03% to 0.1% ointment – 30, 60, 100 gram tubes. Fujisawa Healthcare, Inc.
- Elidel® (Pimecrolimus) 1% cream – 30, 60, 100 gram tubes. Novartis Pharmaceuticals Corp.

Dosage range

- *Mild to moderate short-term to intermittent atopic dermatitis (Eczema)*
  - Recommended use in adults and children over 2 years of age.
  - Elidel® (Pimecrolimus) applied thinly over affected area rubbed in gently twice daily until resolution of symptoms. Discontinuation of treatment should occur after symptoms resolve.
- *Moderate to severe short-term to intermittent atopic dermatitis (Eczema)*
  - Recommended use in children over 2 years of age with the 0.03% ointment. Adults may use either 0.03% or 0.1% ointment.
  - Protopic® (Tacrolimus) applied thinly over affected area rubbed in gently twice daily until resolution of symptoms. Continuation of treatment for 1 week after symptoms resolve.

Known adverse effects/toxicities
Most common adverse effects included: *stinging, burning, soreness, itching, erythema, eczema herpeticum, acne, headache, flu-like symptoms, and increased risk of viral or respiratory infections.*

Black Box Warning – March 10, 2005
There are potential risks with the use of these topical agents as determined by recent animal studies and post-marketing case reports. Systemic formulations of these drugs have shown to be associated with systemic cancers; such as lymphoma and skin papillomas. Topical dosage forms tend to have less systemic absorption but relatively similar carcinogenic risks which increase with duration and level of exposure to these immunosuppressants. The FDA's Pediatric Advisory Committee advised that the dose-dependent risk of developing cancers warrant strict adherence to prescribing Elidel® (Pimecrolimus) and Protopic® (Tacrolimus) only as directed by package insert.

Drug interactions

- Ethanol consumption may exacerbate localized flushing of affected area with tacrolimus use.
- Grapefruit juice and grapeseed extract may inhibit the metabolism through the CYP3A4 inhibition.

Special precautions

Pregnant and breastfeeding women should not use due to the ability to cross into the placenta and breast milk with concentrations similar to or greater than plasma concentrations.

The use of these agents is not recommended with patients diagnosed with Netherton's syndrome which may result in higher systemic absorption.

Lymphadenopathy during treatment should be thoroughly evaluated for the exact etiology to determine possible lymphoma and to choose appropriate treatment.

Treatment is not recommended on active cutaneous viral infections

Non-Pharmacologic Treatments of Atopic Dermatitis

- Proper bathing and utilization of topical moisturizers to treat dry skin is essential in controlling atopic dermatitis.
- Prevent exposure to identified allergens.
- Avoid prolonged exposure to UV light.
- Minimize exposure to extreme temperatures and humidity
- Several homeopathic treatments over-the-counter
- Stress reduction therapy
- Dietary restriction of eggs

Cost Comparison of Atopic Dermatitis Treatments

Agent#	Drug	Purpose	Side-effect profile	Cost*
Topical Corticosteroid (high, medium, low potency)	Clobetasol 0.05% (crm, ont, gel)	Anti-inflammatory; *super-high potency*	Skin Atrophy Hypopigmentation Systemic Effects	$32.99
	Fluocinonide 0.05% (crm, ont, gel)	Anti-inflammatory; *med-high potency*		$27.66
	Fluocinolone acetonide 0.025% (ointment)	Anti-inflammatory; *medium potency*		$9.16
1st Line	Prednicarbate 0.1% (crm,ont)	Anti-inflammatory; *medium-low potency*		$43.30
	Flurandrenolide 0.025% (crm,ont)	Anti-*inflammatory; low* potency		$22.33
	Hydrocortisone 1% (crm,ont)	Anti-inflammatory; *lowest potency*		$3.12
Topical Calcineurin Inhibitors	Pimecrolimus 1% (cream)	Anti-inflammatory; immunosuppressant	Burning, stinging, pruritis, erythema, cancer risk	$57.84
2nd Line	Tacrolimus 0.1% (ointment)			$61.72
	Tacrolimus 0.03% (ointment)			$59.53

*Based on one 30 gram tube. No rebate information was incorporated. #Monotherapy or adjunctive therapy.

Adjunctive Pharmacologic Therapy

- H_1-antihistamines-relieve pruritus.
- Bactroban-antistaphylococcal antibiotic.
- Prednisone-oral corticosteroid for acute exacerbations only due to possible rebound flaring of inflammation.
- Doxepin <8 day treatment for pruritis
- Phosphodiesterase Inhibitors
- Cyclosporine for severe (AD); limited by side effects
- Coal Tar for inflammation and pruritis

Unapproved or Off-label uses

- Alopecia areata, vitiligo, contact dermatitis, lupus erythematosus, seborrheic dermatitis, psoriasis, acne, and blepharitis.

Utilization in Oklahoma Medicaid

During the period between July 2003 and June 2004 a total of 6,888 clients had claims for topical immunosuppressant drugs paid through the Medicaid Fee-for-Service program.

Drugname	Total Claims	Total Units	Total Days	Clients	Total Paid
Elidel Cream 1%	10,758	531,825	149,280	6327	$ 899,322.83
Protopic Ointment 0.03%	582	26,050	8,315	350	$ 50,174.27
Protopic Ointment 0.1%	823	48,780	11,941	390	$ 98,622.48
TOTAL	**12,163**	**606,655**	**169,536**	**6,888***	**$ 1,048,119.58**

*Unduplicated clients for time period.

Both Elidel® and Protopic® are approved for children 2 years of age and older.

Age and Gender FY04

Age	Female	Male	Total
0 to 9	2,290	2,671	4,961
10 to 19	564	377	941
20 to 34	138	26	164
35 to 49	126	65	191
50 to 64	120	67	187
65 to 79	176	59	235
80 to 94	151	41	192
> 95	15	2	17
Total	**3,580**	**3,308**	**6,888**

Topical calcineurin inhibitors are indicated only for short-term intermittent usage and not continuous therapy.

Claims per Recipient for Elidel® and Protopic® FY04

Claim Count	Clients	Percent
1 to 5	6,667	96.79
6 to 10	185	2.69
11 to 15	28	0.41
16 to 20	3	0.04
> 21	5	0.07
Total	**6,888**	**100.00**

Claims per Age ≤ 2 years of Age

	<1 yr	1 yr	2 yr
Female	488	420	338
Male	687	581	369
Total	1175	1001	707

Recommendations

The College of Pharmacy recommends prior authorization for these second-line treatments for atopic dermatitis (eczema) to ensure proper FDA-approved use and to minimize potentially harmful effects documented in recent FDA reports which subsequently led to black box warnings placed on both Elidel® (pimecrolimus) and Protopic® (tacrolimus).

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APPENDIX I

U.S. Food and Drug Administration

FDA News

FOR IMMEDIATE RELEASE
P05-21
April 28, 2005

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

GlaxoSmithKline Signs Consent Decree with FDA; Agrees to Correct Manufacturing Deficiencies

The U.S. Food and Drug Administration (FDA) today announced that GlaxoSmithKline, Inc. (GSK), (through its U.S. subsidiaries SB Pharmco Puerto Rico, Inc., GlaxoSmithKline Puerto Rico Inc., and SmithKline Beecham Corporation), has signed a consent decree with FDA to correct manufacturing deficiencies at its Cidra, Puerto Rico facility.

FDA is concerned that GSK's violation of manufacturing standards may have resulted in the production of drug products that could potentially pose risks to consumers.

The Decree requires GSK to post a penal bond of $650,000,000 contingent upon GSK's either successfully reconditioning drugs seized in March 2005 or destroying them and paying costs to the government.

"The consent decree shows that FDA is serious about enforcing the manufacturing standards essential for safe and effective prescription drugs," said John Taylor, FDA Associate Commissioner for Regulatory Affairs. "It should also reassure the American people that we are doing everything we can to preserve the integrity of the American drug supply."

FDA's last inspection found Paxil CR tablets, approved to treat depression and panic disorder, could split apart. This deficiency could cause patients to receive a portion of the tablets that lacks any active ingredient, or alternatively a portion that contains an active ingredient and does not have the intended controlled-release effect. Additionally, FDA found that some Avandamet tablets, used to treat Type II diabetes, did not have an accurate dose of rosiglitazone, an active ingredient in this product.

The FDA urges patients who use these two drugs to continue taking their medication and to talk with their health care provider about possible alternative products until the manufacturing issues have been resolved.

Under the terms of this decree the company has agreed to take measures to ensure that its Cidra facility and the two drugs, Paxil CR and Avandamet, fully comply with current Good Manufacturing Practice (cGMP) requirements and to ensure that ongoing shipments have the quality attributes they are required to possess. The decree also requires that all corrections and the firm's compliance with cGMP requirements be certified by a third-party expert. Additionally, FDA will continue to monitor these activities through its inspections.

The Decree was presented yesterday for consideration by the United States District Court for the Eastern District of North Carolina. The Decree will take effect after it has been signed and entered by the Court.

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RSS Feed for FDA News Releases

Alert for Healthcare Professionals
Tacrolimus (marketed as Protopic)

FDA Alert [03/2005]:

The FDA has issued a public health advisory to inform healthcare professionals and patients about a potential cancer risk from use of Protopic (tacrolimus). This concern is based on information from animal studies, case reports in a small number of patients, and knowledge of how drugs in this class work. It may take human studies of ten years or longer to determine if use of Protopic is linked to cancer. In the meantime, this risk is uncertain, and FDA advises Protopic should be used only as labeled, for patients after other prescription treatments have failed to work or cannot be tolerated.

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

To report any unexpected adverse or serious events associated with the use of Protopic, please contact the FDA MedWatch program at 1-800-FDA-1088 or http://www.fda.gov/medwatch/report/hcp.htm

Recommendations

Physicians with patients using Protopic, or who are considering prescribing the drug, should consider the following:

- Use Protopic only as **a second-line** agent for short-term and intermittent treatment of atopic dermatitis, a form of eczema, in patients unresponsive to, or intolerant of other treatments.
- Avoid use Protopic in children younger than 2 years of age. The effect of Protopic on the developing immune system in infants and children is not known.
- Use Protopic only for short periods of time, not continuously. The long term safety of Protopic is unknown.

- Children and adults with a weakened or compromised immune system should not use Protopic.

- Use the minimum amount of Protopic needed to control the patient's symptoms. In animals, increasing the dose resulted in higher rates of cancer.

Data Summary

Although tacrolimus is not genotoxic and does not interact directly with DNA, it may have a potential to impair local immunosurveillance. Carcinogenicity studies conducted with topical application of tacrolimus in mice demonstrated a dose-dependent development of lymphoma. The systemic administration of tacrolimus in kidney and liver transplant patients has been associated with increased susceptibility to infection and development of lymphoma and skin malignancies.

As of December 2004, the FDA had received 19 cases of postmarketing reports linking Protopic with cancer-related adverse events. Three cases occurred in children up to 16 years of age, and 16 cases occurred in adults. Two deaths in adults were reported related to complications of the cancers, and 8 hospitalizations were reported, including 2 in pediatric patients.

The 19 postmarketing cases included 9 lymphomas, 10 cutaneous tumors, of which 7 occurred at the site of Protopic application, as well as cases of squamous cell carcinoma, cutaneous sarcoma, malignant melanoma and other tumor types. The median time until diagnosis after initiation of treatment with Protopic was 150 days, with a range between 21 days and 790 days. Six cases also reported lymphadenopathy. Two cases reported pre-existing serious conditions, and 4 cases reported a recurrence or aggravation of a pre-existing malignancy. Three additional cases were confounded by other possible risk factors, including environmental exposure, or pre-existing conditions that may have been pre-malignant.

The systemic form of tacrolimus (Prograf) is known to cause both skin cancers and lymphoma in humans by suppressing the body's normal immune defenses against cancer. The cancer risk increases with higher doses and longer treatment courses of Prograf. Protopic is sometimes absorbed through the skin, though usually at very low amounts. Occasionally, children who have been treated with Protopic have had measurable blood levels of the drug, in the range of patients treated with Prograf. The potential for systemic immunosuppression is unknown and the role of Protopic in the development of the cancer-related events in the individual postmarketing cases is also uncertain.

FDA Patient Information Sheet
http://www.fda.gov/cder/drug/InfoSheets/patient/ProtopicPIS.pdf

Report serious adverse events to FDA's MedWatch at 1-800-FDA-1088; or
http://www.fda.gov/medwatch/report/hcp.htm

Questions? Call Drug Information, 1-888-INFO-FDA (automated) or 301-827-4570
Druginfo@cder.fda.gov

Back to Top Back to Protopic

Alert for Healthcare Professionals
Pimecrolimus (marketed as Elidel)

FDA ALERT [03/2005]:

The FDA has issued a public health advisory to inform healthcare professionals and patients about a potential cancer risk from use of Elidel (pimecrolimus). This concern is based on information from animal studies, case reports in a small number of patients, and knowledge of how drugs in this class work. It may take human studies of ten years or longer to determine if use of Elidel is linked to cancer. In the meantime, this risk is uncertain, and FDA advises Elidel should be used only as labeled, for patients after other prescription treatments have failed to work or cannot be tolerated.

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

To report any unexpected adverse or serious events associated with the use of Elidel, please contact the FDA MedWatch program at 1-800-FDA-1088 or http://www.fda.gov/medwatch/report/hcp.htm

Recommendations

Physicians with patients using Elidel, or who are considering prescribing the drug, should consider the following:

- Use Elidel only as **second-line** agent for short-term and intermittent treatment of atopic dermatitis, a form of eczema, in patients unresponsive to, or intolerant of other treatments.
- Avoid use of Elidel in children younger than 2 years of age. The effect of Elidel on the developing immune system in infants and children is not known. In clinical studies, infants and children younger than 2 years old treated with Elidel had a higher rate of upper respiratory infections than those treated with placebo cream.

- Use Elidel only for short periods of time, not continuously. The long term safety of Elidel is unknown.
- Children and adults with a weakened or compromised immune system should not use Elidel.
- Use the minimum amount of Elidel needed to control the patient's symptoms. In animals, increasing the dose resulted in higher rates of cancer.

Data Summary

Although pimecrolimus is not genotoxic and does not interact directly with DNA, it may have a potential to impair local immunosurveillance. Repeat dose studies conducted with topical application of pimecrolimus in mice demonstrated a dose and treatment dependent development of lymphoma. Carcinogenicity studies conducted with oral administration of pimecrolimus in mice demonstrated a dose dependent development of lymphoma and benign thymoma. Carcinogenicity studies conducted with topical administration of pimecrolimus in rats demonstrated development of follicular cell adenoma of the thyroid. Data from a recently conducted oral nine-month monkey study showed a dose-related increase in virus-associated lymphoma following administration of pimecrolimus.

As of December 2004, the FDA had received 10 cases of postmarketing reports linking Elidel with cancer-related adverse events. Four cases occurred in children, 3 of these in children less than 6 years of age. The other 6 cases occurred in adults.

Of the 10 postmarketing cases reporting cancer, 6 described cutaneous tumors, 1 described a lymph node/cutaneous tumor related event, and the locations of 3 others were unreported. Four cases described lymphomas; 5 cases described a variety of tumors, including basal cell carcinoma and squamous cell carcinoma; and 1 case described granulomatous lymphadenitis. The median time until diagnosis after initiation of treatment with Elidel was 90 days, with a range between 1 week and 300 days. Two cases also reported a lymphadenopathy. Two cases were confounded, 1 with the presence of nodules prior to the diagnosis of basal cell carcinoma; and another with a pre-existing condition associated with an increased risk for malignant transformation.

Elidel is sometimes absorbed through the skin, though usually at very low amounts. Occasionally, children who have been treated with Elidel have had measurable blood levels of the drug. The potential for systemic immunosuppression is unknown and the role of Elidel in the development of the cancer-related events in the individual postmarketing cases is also uncertain.

FDA Patient Information Sheet
http://www.fda.gov/cder/drug/InfoSheets/patient/ElidelPIS.pdf

Questions? Call Drug Information, 1-888-INFO-FDA (automated) or 301-827-4570
Druginfo@cder.fda.gov

Back to Top Back to Elidel

Date created: February 14, 2005, updated March 30, 2005

U.S. Food and Drug Administration

FDA Talk Paper

T05-13
April 11, 2005

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

FDA Issues Public Health Advisory for Antipsychotic Drugs used for Treatment of Behavioral Disorders in Elderly Patients

The Food and Drug Administration (FDA) today issued a public health advisory to alert health care providers, patients, and patient caregivers to new safety information concerning an unapproved (i.e., "off-label") use of certain drugs called "atypical antipsychotic drugs." These drugs are approved for the treatment of schizophrenia and mania, but clinical studies of these drugs to treat behavioral disorders in elderly patients with dementia have shown a higher death rate associated with their use compared to patients receiving a placebo (sugar pill).

Today's advisory applies to such antipsychotic drugs as Abilify (aripiprazole), Zyprexa (olanzapine), Seroquel (quetiapine), Risperdal (risperidone), Clozaril (clozapine) and Geodon (ziprasidone). Symbyax, which is approved for treatment of depressive episodes associated with bipolar disorder is also included in the agency's advisory.

FDA is requesting that the manufacturers of all of these kinds of drugs add a boxed warning to their drug labeling describing this risk and noting that these drugs are not approved for the treatment of behavioral symptoms in elderly patients with dementia. Patients receiving these drugs for treatment of behavioral disorders associated with dementia should have their treatment reviewed by their health care providers.
In analyses of seventeen placebo-controlled studies of four drugs in this class, the rate of death for those elderly patients with dementia was about 1.6 to 1.7 times that of placebo. Although the causes of death were varied, most seemed to be either heart-related (such as heart failure or sudden death) or from infections (pneumonia).

The atypical antipsychotics fall into three drug classes based on their chemical structure. Because the increase in mortality was seen with atypical antipsychotic medications in all three chemical classes, the agency has concluded that the effect is probably related to the common pharmacologic effects of all atypical antipsychotic medications, including those that have not been studied in the dementia population.

The agency is considering adding a warning to the labeling of older antipsychotic medications because limited data also suggest a similar increase in mortality for these drugs. The review of the data on these older drugs, however, is still on-going.

Additional information concerning today's announcement is available on FDA's Web site at http://www.fda.gov/cder/drug/infopage/antipsychotics/default.htm and http://www.fda.gov/cder/drug/advisory/antipsychotics.htm.

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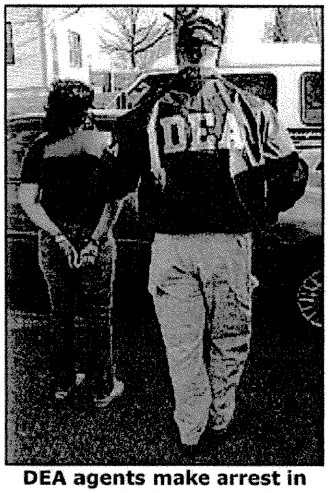
News Release
FOR IMMEDIATE RELEASE
Contact: DEA Public Affairs
202-307-7977
April 20, 2005

International Internet Drug Ring Shattered

E-Traffickers Arrested: Indian/Costa Rican/Canadian Cyber Criminal Alliances Shut Down



DEA agents make arrest in New York portion of Operation "Cyber Chase."

Drug Enforcement Administration (DEA) Administrator Karen P. Tandy today announced the results of Operation "Cyber Chase", a year-long Organized Crime Drug Enforcement Task Force (OCDETF) investigation that targeted international Internet pharmaceutical traffickers operating in the United States, India, Asia, Europe and the Caribbean. These e-traffickers distributed drugs world-wide using "rogue" Internet pharmacies.

Over the past 48 hours there were 20 arrests in eight U.S. cities and four foreign countries. Domestically arrests occurred in Philadelphia, Pennsylvania; Ft. Lauderdale and Sarasota, Florida; Abilene and Tyler, Texas; New York, NY; Greenville, SC; and Rochester, New York. Internationally arrests occurred in San Jose, Costa Rica; New Delhi, Agra, and Bombay, India.

DEA Administrator Tandy; Scott Burns Deputy Director for State and Local Affairs, White House Office of National Drug Control Policy (ONDCP); Brian Lampkin, Section Chief, Federal Bureau of Investigation (FBI), Financial Crimes Section; Deputy Assistant Director of Investigations of U.S. Immigration and Customs Enforcement (ICE) Paul Kilcoyne; Associate Commissioner for Regulatory Affairs, Food and Drug Administration, John M. Taylor; Paul J. Trimbur, Inspector in Charge, Mail Theft, Violent Crimes and Narcotics Investigations, U.S. Postal Inspections Service (USPIS); and Commissioner Mark W. Everson, Internal Revenue Service (IRS) made the announcement today.

DEA, FBI, ICE, FDA, USPIS, IRS, United States Attorney for the Eastern District of Pennsylvania Patrick L. Meehan; United States Attorney for the Eastern District of New York Roslynn R. Mauskopf; state and local law enforcement; and law enforcement authorities in four foreign countries participated in this investigation.

Operation "Cyber Chase" targeted major pharmaceutical drug traffickers who allegedly shipped Schedule II-V pharmaceutical controlled substances including narcotics, amphetamines, and anabolic steroids directly to buyers of all ages without the medical examination by a physician required by U.S. law.

These e-traffickers used more than 200 websites to illicitly distribute pharmaceutical controlled substances. Cyber Chase is part of DEA's "On-Line Pharmacy Investigation Strategy" spearheaded by DEA's Special Operations Division (SOD). SOD is a joint law enforcement program which is comprised of agents and analysts from the DEA, FBI, IRS and ICE, as well as attorneys from the Department of Justice's Criminal Division.

DEA Administrator Karen P. Tandy said, "For too long the Internet has been an open medicine cabinet with cyber drug dealers illegally doling out a vast array of narcotics, amphetamines, and steroids. In this first major international enforcement action against online

rogue pharmacies and their sources of supply, we've logged these traffickers off the Internet."

Operation Cyber Chase began after the DEA Philadelphia Division identified a Philadelphia-based international Internet drug trafficking organization, allegedly headed by Indian nationals Brij Bhusan Bansal and Akhil Bansal. The Bansal Organization allegedly repackaged controlled substances smuggled into the United States from India and other countries and distributed them throughout the U.S. and the world.

John Walters, Director of National Drug Control Policy said, "Prescription drugs help millions of Americans every day. But their misuse is becoming a serious problem, abetted by drug traffickers who are using the Internet to attempt to subvert our medical prescription system. E-traffickers that target young people and those suffering from the disease of addiction are now the target of law enforcement action, while we continue to ensure proper access to needed medications. I would like to thank and applaud the agencies and offices involved in this investigation as their efforts truly make America safer."

Since July 2003, the Bansal Organization distributed approximately 2.5 million dosage units of Schedule II-V pharmaceutical controlled substances including Vicodin (hydrocodone), anabolic steroids, and amphetamines per month.

"The FBI remains committed to investigating the illegal sale of pharmaceuticals over the Internet. The FBI's Internet Pharmaceutical Fraud Initiative is working with the Drug Enforcement Administration, and other federal, state, local and international law enforcement partners to combat this crime and dismantle the responsible criminal enterprises," said FBI Director Robert Mueller. "Illegal pharmaceuticals pose a great risk to the health and welfare of the American public. These drugs are being manufactured overseas in unregulated facilities, smuggled into the United States in an uncontrolled environment, and distributed without oversight of a licensed physician or pharmacist."

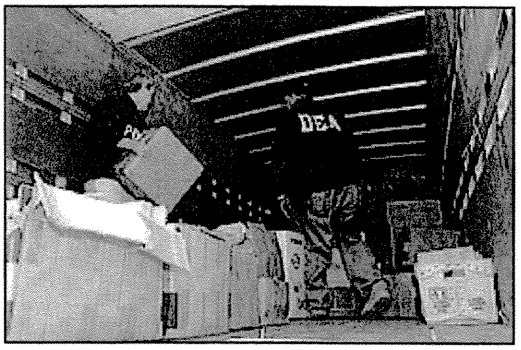
"This investigation dismantled a major source of illicit pharmaceuticals that posed a significant public health threat. Closing down these illegal, Internet drug pipelines is essential to protecting consumers of pharmaceuticals," said Michael J. Garcia, Assistant Secretary, Immigration and Customs Enforcement.

"Operation Cyber Chase sends an instant message to 'cybercriminals' that the Internet is not their safehouse. Criminals, disguised as entrepreneurs, use the Internet to invade your home and push their poison. Whether the battle is on the street or on the Web, the outcome remains the same: Postal Inspectors will continue working with our law enforcement partners to bring offenders to justice," said Chief Postal Inspector Lee R. Heath.

"Consumers ordering prescription drugs from a website they're not familiar with put themselves in a 'buyer beware' situation," said John Taylor, Associate Commissioner for Regulatory Affairs, Food and Drug Administration. "The medications may be coming from unknown sources, may not be stored or labeled properly, and may not meet quality assurance standards designed to produce safe and effective products. Many of the safeguards that exist for brick and mortar pharmacies do not exist for Internet Pharmacies and the potential for harmful drug interactions is magnified."

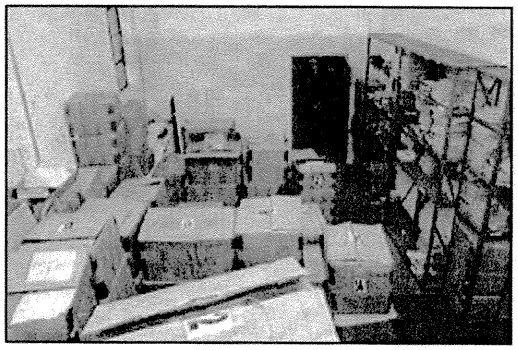
"The combined efforts of law enforcement agencies in an investigation of this magnitude produce a formidable force against narcotics trafficking and money laundering. Individuals and businesses utilizing the Internet to sell pharmaceuticals are bound by the same laws and regulations that apply to the corner drug store," said Nancy Jardini, Chief, IRS Criminal

Investigation. "The link between where the money comes from, who gets it, when it is received, and where it is stored or deposited, can provide evidence that a crime was committed. Finding and connecting those links is what IRS brings to this cooperative effort."



In early April, the Grand Jury in the Eastern District of Pennsylvania and in the Eastern District of New York issued indictments charging the following: 21 U.S.C. § 841 Illegal Distribution of Controlled Substances, 21 U.S.C. § 846 Conspiracy to Distribute Controlled Substances, 21 U.S.C. § 848 Continuing Criminal Enterprise, 21 U.S.C. § 963 Conspiracy to Import Controlled Substances, 21 U.S.C. § 331(a) Introduction of Misbranded Drugs into Interstate Commerce, 18 U.S.C. § 1956(h) Conspiracy to Commit Money Laundering, 18 U.S.C. § 1956 (a)(1) Promotional Money Laundering, 18 U.S.C. § 1956(a)(2) International Money Laundering, 18 U.S.C. § 1957 Transactional Money Laundering, 18 U.S.C. § 982 Criminal Forfeiture, 21 U.S.C. § 853 Criminal Forfeiture, 21 U.S.C. § 970 Criminal Forfeiture and 18 U.S.C. § 2 Aiding and Abetting

This indictment also seeks forfeiture of 41 bank accounts, 26 in the U.S. and the remaining in Cyprus, India, Singapore, the Channel Islands, Isle of Man, West Indies, Antigua, and Ireland. Illegal financial transactions listed in the indictment total more than $6 million with restitution sought for that amount.



During January 2005, DEA launched a toll-free international hotline—1-877-RxAbuse for the public to anonymously report the illegal sale and abuse of prescription drugs. DEA has received hundreds of tips already, including those about suspicious Internet pharmacies, and this information is assisting DEA to bring drug dealers to justice.

The following foreign and domestic agencies participated in Operation Cyber Chase:

Domestic

LOCATION	ENTITY
Philadelphia	Drug Enforcement Administration Internal Revenue Service Immigration and Customs Enforcement Federal Bureau of Investigation, Healthcare Fraud Food and Drug Administration United States Postal Service Chester City Police Department Delaware County CID
New York	DEA Rochester – DEA Food and Drug Administration Immigration and Customs Postal Inspectors New York Police Department
Long Island	DEA
Special Operations Division Department of Justice	Pharmaceutical and Chemical Coordination Unit Narcotics and Dangerous Drug Section

Foreign

LOCATION	ENTITY
Australia	DEA - Canberra Australian Federal Police
India	DEA - New Delhi Narcotics Control Bureau
Costa Rica	DEA
Canada	Royal Canadian Mounted Police

*****B-Roll footage available*****
*****Spanish-speaking DEA representatives available for interviews*****
***** Administrator Tandy's recorded audio actualities regarding this agreement can be accessed by calling 888-557-6494. When prompted, dial 713, 714, 715, and 716 (You will need to dial separately for each recorded comment)*****