THE UNIVERSITY OF OKLAHOMA

MEMORANDUM

TO: Drug Utilization Review Board Members

FROM: Shellie Gorman, Pharm.D.

SUBJECT: **Packet Contents for Board Meeting – August 13, 2008**

DATE: August 6, 2008

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

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

Call to Order

Public Comment Forum

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

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

Action Item – Vote to Prior Authorize Voltaren® Gel – **See Appendix C.**

30 Day Notice to Prior Authorize Erythropoiesis Stimulating Agents – **See Appendix D.**

30 Day Notice to Prior Authorize Patanase® – **See Appendix E.**

Action Item – Annual Review of Antiulcer PBPA category and 30 Day Notice to Prior Authorize Protonix® Suspension – **See Appendix F.**

Action Item – Qualaquin® Annual Review – **See Appendix G**

White Paper on Bioequivalent Medications – **See Appendix H.**

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

Future Business

Adjournment

Drug Utilization Review Board

(DUR Board)

Meeting – August 13, 2008 @ 6:00 p.m.

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. McNeill, Chairman:

1. Call To Order

A. Roll Call – Dr. Graham

Items to be presented by Dr. McNeill, Chairman:

2. Public Comment Forum

A. Acknowledgment of Speakers and Agenda Item

Items to be presented by Dr. McNeill, Chairman:

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

A. July 9, 2008 DUR Minutes – Vote
B. July 10, 2008 DUR Recommendations Memorandum
C. Provider Correspondence

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

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

A. Retrospective Drug Utilization Review for April 2008
B. Retrospective Drug Utilization Review Responses for January 2008
C. Medication Coverage Activity Audit for July 2008
D. Help Desk Activity Audit for July 2008

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

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

A. Product Summary
B. COP Recommendations

Drug Utilization Review Board

(DUR Board)

Meeting – August 13, 2008 @ 6:00 p.m.

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Meece, Vice-Chairman:

1. Call To Order

A. Roll Call – Dr. Graham

Items to be presented by Dr. Meece, Vice-Chairman:

2. Public Comment Forum

A. Acknowledgment of Speakers and Agenda Item

Items to be presented by Dr. Meece, Vice-Chairman:

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

A. July 9, 2008 DUR Minutes – Vote
B. July 10, 2008 DUR Recommendations Memorandum
C. Provider Correspondence

Items to be presented by Dr. Keast, Dr. Meece, Vice-Chairman:

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

A. Retrospective Drug Utilization Review for April 2008
B. Retrospective Drug Utilization Review Responses for January 2008
C. Medication Coverage Activity Audit for July 2008
D. Help Desk Activity Audit for July 2008

Items to be presented by Dr. Patel, Dr. Meece, Vice-Chairman

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

A. Product Summary
B. COP Recommendations

Items to be presented by Dr. Keast, Dr. Meece, Vice-Chairman:

6. 30 Day Notice to Prior Authorize Erythropoiesis Stimulating Agents – See Appendix D.

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

Items to be presented by Dr. Browning, Dr. Meece, Vice-Chairman

7. 30 Day Notice to Prior Authorize Patanase® – See Appendix E.

A. Product Summary
B. COP Recommendations

Items to be presented by Dr. Moore, Dr. Meece, Vice-Chairman

8. Action Item – Annual Review of Antiulcer PBPA Category and 30 Day Notice to Prior Authorize Protonix® Suspension – See Appendix F.

A. Current PA Criteria
B. Utilization Review
C. COP Recommendations

Items to be presented by Dr. Patel, Dr. Meece, Vice-Chairman

9. Action Item – Qualaquin® Annual Review – See Appendix G.

A. Product Summary
B. Current PA Criteria
C. Utilization Review
D. COP Recommendations

Items to be presented by Dr. Le, Dr. Meece, Vice-Chairman

10. White Paper on Bioequivalent Medications – See Appendix H.

A. White Paper
B. FDA MedWatch Form

Items to be presented by Dr. Graham, Dr. Meece, Vice-Chairman

11. FDA and DEA Updates – See Appendix I.

12. Future Business

A. Antidepressants
B. Oral Antifungals Utilization Review
C. Hemophilia Review
D. Annual Reviews
F. Glaucoma Intervention Report
G. New Product Reviews

13. Adjournment

Appendix A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of JULY 9, 2008

BOARD MEMBERS:	PRESENT	ABSENT
Brent Bell, D.O., D.Ph.	X	
Jay D. Cunningham, D.O.	X	
Mark Feightner, Pharm.D.	X	
Dorothy Gourley, D.Ph.	X	
Evelyn Knisely, Pharm.D.		X
Thomas Kuhls, M.D.	X	
Dan McNeill, Ph.D., PA-C; Chairman	X	
Cliff Meece, D.Ph.; Vice-Chairman	X	
John Muchmore, M.D., Ph.D.	X	
James Rhymer, D.Ph	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	
Shellie Keast, Pharm.D.; DUR Manager	X	
Ronald Graham, D.Ph.; Pharmacy Director	X	
Chris Le, Pharm.D.; Clinical Pharmacist/Coordinator	X	
Carol Moore, Pharm.D.; Clinical Pharmacist	X	
Neeraj Patel, Pharm.D.; Clinical Pharmacist	X	
Lester A. Reinke, Ph.D.; Associate Dean for Graduate Studies & Research	X	
Visiting Pharmacy Students: Lisa Huggins, Michael Appiah	X	

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Mike Fogarty, J.D., M.S.W.; Chief Executive Officer		X
Nico Gomez; Director of Gov't and Public Affairs		X
Lynn Mitchell, M.D., M.P.H,; Director of Medicaid/Medical Services	X	
Nancy Nesser, Pharm.D., J.D.; Pharmacy Director		X
Howard Pallotta, J.D.; Director of Legal Services		X
Lynn Rambo-Jones, J.D.; Deputy General Counsel III	X	
Rodney Ramsey; Drug Reference Coordinator	X	
Jill Ratterman, D.Ph.; Pharmacy Specialist		X
Kerri Wade, Senior Pharmacy Financial Analyst	X	

OTHERS PRESENT:

Stephen McFadden, Forest Labs	David Williams, Forest Labs	Jim Dunlap, Eli Lilly
Sam Smothers, MedImmune	Brian Fulkerson, MedImmune	Marland Thurman, Eli Lilly
Mellelo Kort, Eli Lilly	Mario Munoz, Eli Lilly	Brenan Fulkerson, MedImmune
Fran Lasiter, Forest	Kat Daniel, Forest	Aaron Mays, Alcon
Damon Williams, Wyeth	Cathy Hollen, Eli Lilly	Pat Trahan, Taro
Lisa Buck, Pfizer	Paul Davies, MHAT	James Lieurance, Endo Pharmaceuticals
Lara Stewart, Merck	Susie Seymour, OMHCC	Jim Graham, J&J
Jacque Collier, Abbott	Toby Thompson, Pfizer	Randy Clifton, Amgen
Bobby White, UCB	Susan Stone, Allergan	Sandy Pruitt, DBSA-OK
Laura Mitchell, Purdue Pharma	Mark DeClerk, Lilly	Vince Morrison, Forest
Linda Cantu, BMS	Donna Erwin, BMS	Jorge Nasser, BMS
Janie Huff, Takeda	Carlos Palasciano, Hawthorn	John Walker, Wyeth
Rebecca King, Taro	John Bozalis, Okla. Allergy/Asthma Clinic	

PRESENT FOR PUBLIC COMMENT:

Agenda Item No. 9:	Felecia Williams, Merck; Norman Imes, MD, private practice
Agenda Item No. 10:	Pauline Patrick, Forest Labs; Khalil Saliba, MD, Laureate Psych. Hospital; Susie Seymour, OMHCC; Art Rousseau, MD, Okla. Psychiatric Phys. Assoc.; Leland Dennis, MD, private practice
Agenda Item No. 11:	James Lieurance, Endo Pharmaceuticals

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

1A: Roll Call

Dr. Meece called the meeting to order. Roll call by Dr. Graham established a quorum.

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 2: **PUBLIC COMMENT FORUM**

Dr. McNeill recognized the speakers for public comment.

Agenda Item No. 9: Felecia Williams, Merck; Norman Imes, MD, private practice

Agenda Item No. 10: Pauline Patrick, Forest Labs; Khalil Saliba, MD, Laureate Psych. Hospital; Susie Seymour, OMHCC; Art Rousseau, MD, Okla. Psychiatric Phys. Assoc.; Leland Dennis, MD, private practice

Agenda Item No. 11: James Lieurance, Endo Pharmaceuticals

ACTION: NONE REQUIRED.

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

3A: May 14, 2008 DUR Minutes

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

ACTION: MOTION CARRIED.

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

4A: Retrospective Drug Utilization Review Report: February 2008
4B: Retrospective Drug Utilization Review Report: March 2008
4C: Retrospective Drug Utilization Review Responses: November 2007
4D: Retrospective Drug Utilization Review Responses: December 2007
4E: Medication Coverage Activity Audit: May 2008
4F: Medication Coverage Activity Audit: June 2008
4G: Help Desk Activity Audit: May 2008
4H: Help Desk Activity Audit: June 2008

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

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 5: **VOTE TO PRIOR AUTHORIZE OSTEOPOROSIS MEDICATIONS**

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

Teriparatide may be used after a minimum 12 month trial with a bisphosphonate plus adequate calcium and vitamin D (unless contraindicated, intolerant, or allergic) and a BMD (T-score at or below -2.5) test within the last month

Dr. Muchmore moved to approve as amended; seconded by Dr. Meece.

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE TOPICAL ANTIBIOTICS**

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

Dr. Kuhls moved to approve as submitted; seconded by Dr. Gourley.

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE AURALGAN™**

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

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

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 8: **VOTE TO PRIOR AUTHORIZE PLAVIX® 300 MG**

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

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

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 9: **VOTE TO PRIOR AUTHORIZE SINGULAIR®**

For Public Comment, Felecia Williams: I'm Felecia Williams, a pediatrician and regional medical director with Merck. Prior to joining Merck in December 2007 I was a hospital administrator serving in various roles including chief operating officer (unintelligible) medical director. Prior to that time I practiced pediatrics in Detroit, Michigan where I served a predominantly Medicaid population where asthma, allergic rhinitis, ectopic dermatitis and other related conditions constituted approximately 15% of my practice. I'm speaking today in support of Singulair, specifically I would like you to reconsider the PA that has been recommended. The efficacy of Singulair has been established in numerous clinical trials and it has been found to increase lung function as demonstrated by improvements in FEV_1, decreasing the need for rescue medications and decreased asthma attacks and improved symptoms associated with both asthma and allergic rhinitis. Current asthma guidelines emphasize control as the key goal for patients with asthma. The guidelines recommend portraying separate antagonists as an alternative to inhaled corticosteroid as controller therapy in patients with mild persistent asthma. In patients with more severe asthma, Singulair has also been shown to improve lung function and to allow reduction in steroid dose. The use of Singulair as an alternative controller medication is important because of the heterogeneity of asthma. Clinical expression can vary from one patient to another as some patients will respond to both medications and some patients will respond to either medication. However a large percentage of patients, non-responders, will respond to neither medication. Some studies have shown to upward of 55%. So given the goal of control which includes the decreasing risk impairment and the heterogeneity of the disease, physicians and healthcare professionals caring for patients with asthma must have therapeutic options and the ability to individualize therapy. Actually, the ability to individualize treatment plans, taking into consideration those patients who may have difficulty with adherence or inhaler technique or where inhaled corticosteroids may not be appropriate. Adherence to controller medication is critical as these medications are very effective in decreasing chronic inflammation which is the hallmark of asthma. The current PA recommendations requiring a diagnosis of asthma will create significant barriers and possibly unintended consequences for patients newly diagnosed with asthma. Physicians and healthcare professionals are often reluctant to give patients the diagnosis of asthma. Patients with symptoms of asthma may be given a diagnosis of bronchialitis, upper respiratory tract infection, bronchitis and reactive airway disease. For these patients who might benefit from Singulair and where Singulair may be a more appropriate drug, there's a potential delay in these patients receiving Singulair. Given the morbidity, mortality and costs associated with asthma, especially in vulnerable populations, I encourage you to not implement these recommendations. I would also ask you that you consider that first impact and additional burdens on families, patients and providers, and possibly unintended consequences of increased utilization with respect to office visits, burden and care visits, emergency department visits and hospitalizations as well as increased drug costs. The impact of allergic rhinitis on asthma symptoms, quality of life, ability to function, behavior and families will be significant. These recommendations, particularly those that require patients to undergo a 14-day trial of both Tier 1 drugs, then a 14-day trial of a Tier 2 drug, especially ..... I'm sorry ..... and a 14-day trial of a Tier 2 drug, essentially six weeks of suffering with AR symptoms, before a patient can receive Singulair are overly burdensome for patients and their families. As you know, a large percentage of patients with asthma also suffer from allergic disease. Additionally, many patients have already tried over-the-counter medications prior to seeking medical attention for allergy symptoms. Please note that the Texas Medicaid program had similar edits for Singulair that began in February 2008, however after realizing the undue burden of such restrictions on families and patients, the edits were removed effective July 1st. Again I implore you to keep Singulair, to keep a Singular status that is unrestricted. Seriously consider the feedback that you have received from physicians who care for these patients. Let's focus on control and avoid the potential unintended consequences of these recommendations which include prolonging symptoms of AR and asthma, increasing impairment and risk and vulnerable population potentially increasing utilization in the ambulatory setting, increasing drug costs as well as impairing physicians' and healthcare professionals' ability to achieve control in these patients. I appreciate your time and consideration. Thank you.

For Public Comment, Norman Imes, MD: I want to hand out a couple of graphs here just to illlustrate a couple of points. The first thing I want to emphasize ..... I might introduce myself. I'm Norman Imes. I have a private practice here in Oklahoma City. I'm a former pulmonologist and critical care doctor. I now do primarily sleep medicine. I don't do much pulmonary any more, but I do have an interest in pulmonary medicine and so I try to keep up in that particular field. I was a little bit concerned about the recommendations because I consider Singulair to be a very important drug in the treatment of my patients over the last fifteen years or so that the drug has been on the market, so I do have a vested interest in what happens here. The primary goals of asthma therapy as you've been advised are primarily to control the patients' symptoms. I think the new guidelines emphasize that. And they emphasize I think a little bit more than they should at the expense of what happens to the FEV_1. I personally still like breathing tests and so on in order to follow my patients, but the new guidelines look primarily at patient symptom control. The leukotriene receptor antagonists has already, has pointed out by Dr. Williams is that many many studies have shown that it does provide asthma control for the patients symptoms. Now the question here is primarily one of, is it better, is it equal to, is it a viable alternative to inhaled corticosteroids. In my opinion, there are really only two controller drugs. A controller drug, in order to be a controller drug, must be an anti-inflammatory drug. There are actually three of them if you consider Xolair, but Xolair is reserved for those patients who have severe asthma, so for the routine asthmatic that we're talking about, we're talking about either inhaled corticosteroids or we're talking about Singulair, and so those are the two drugs that we have to look at. Now if you look at the majority of studies and I know you've got some information here on the background of why this was decided, which I will critique here in a second, that the majority of studies illustrate that the symptom control between inhaled corticosteroids and leukotriene receptor antagonists such as Singulair, are equivalent. What you see that is different is you see that there is a difference in the response to the FEV_1, in other words, pulmonary function

study, which in most cases is not going to be done anyway, but if you're talking about mild persistent asthma then it becomes kind of a non-issue because pulmonary function studies by definition, people that have mild asthma, are basically normal, so it doesn't really come up as a . . . you're really looking at symptom control, and symptom control is equal between the two drugs. So that's the main criticism I have trying to take away one drug as opposed to the other and making it the preferred drug. Now I want to call your attention to this particular graph, which is montelukast versus beclomethasone. I think this is a very important concept. We've had it on our mind sometimes that, gee, the inhaled corticosteroids improve the patients FEV_1 more than the patient who has been taking leukotriene receptor antagonists such as Singulair. The problem is they're both bell shaped curves and most of the improvement that you see statistically, and the difference between the two grooves is related to some patients who do very well who get inhaled corticosteroids. But if you look at absolute numbers of people who have 11% improvement or more, they're actually very close to the same. The inhaled corticosteroids went up by a little bit. Now I know there's also a lot made of the exacerbation rates when you switch people off of inhaled corticosteroids back to leukotriene receptor antagonists such as Singulair. The problem with those studies is the reverse also happens. If you have somebody who's maintained on Singulair and you take them off that and put them on inhaled corticosteroids it has a relapse rate because as has already been mentioned, the failure rate of inhaled corticosteroids, the failure rate of inhaled corticosteroids in treatment of asthma is someplace between 25 and 50%. Pretty astounding. So when you look at this you can see that there is a big failure rate, here's the zero point right here, so it's a big failure rate for both drugs. So you certainly don't want to remove one of your only two controller drugs from your pharmacy. Now as mentioned, the GINA guidelines and the NAEPP guidelines emphasize patient symptom control. And here's a graph using the same patients which are about 650 patients in each of the two groups, Singulair, inhaled steroids and there was another group which had placebo, but that wasn't critical of course to this discussion. If you look at asthma control days, they're actually precisely the same. So asthma control days in patients who get inhaled corticosteroids and patients who get Singulair, in most studies, granted you can pick and choose studies, they're virtually the same. So the reason that the GINA guidelines came up with leukotriene modifying drugs as an alternative, and I notice in the statement here it says that inhaled steroids are recommended as a preferred agent of choice in the guidelines. That's not true. GINA recommends it as an alternative choice in the patient who has mild persistent asthma. So that was a misstatement. Now if you look at these, this information that was presented as the summary of evidence, this was cherry-picked to a large degree. The third study down here which came from the asthma clinical network trials, that study was severely biased. That's the bullet point 1-2-3-4, the last one down here. In that particular trial, guess what, SmithKlineFrench kept right to protocol. They reviewed the protocol. They reviewed the data. So what they did was they selected patients who were going to respond to inhaled corticosteroids the best, so the exacerbation rate was higher in those patients who were placed on montelukast. I don't know how to really interpret that except that they were biased towards the inhaled corticosteroids. However symptom control, despite the fact it was biased, symptom control in all the groups, whether they got inhaled corticosteroids or they got Singulair, was the same. They still got good symptom control. So again, even though it was a biased study, it didn't really prove that the patients did any more poorly. The third bullet point here which has to do with long-acting beta agonists as an alternative, forget it. Long-acting beta agonists are not a second line drug for control of asthma. It's a dangerous drug. There's a plethora of data in the literature that shows that long-acting beta agonists should not be used as second line drugs and that is also borne out by the FDA warning. These drugs such as Advair, Foradil and so on, they all have black box warnings. And there's a reason for that. We won't go into that because we don't have time. So in summary I think it's not prudent to remove one of the two drugs that we have available which are controller drugs, in the treatment of asthma because we have such a high failure rate with patients who are on inhaled corticosteroids. The patients' compliance has been proven to be much better on monotherapy, one drug, you get much better compliance from patients than if you tried to use inhaled corticosteroids. So again, there's a lot of studies which we won't get into here that show that if you get monotherapy, the patient will do better because they take the drug. There's in interesting study and I only found this one study, in which they looked at a Medicare population in North Carolina and they looked at the same issue. If the patient was relegated to taking Singulair versus inhaled corticosteroids, what was the health care cost ..... was there a savings by using inhaled corticosteroids. The answer was "no". They were the same. Why? Because even though you might have made an argument that the control should have been better with inhaled corticosteroids, it was not. Probably because they weren't using the drug. So there's a big positive here because the patients do have monotherapy, one pill a day. Also you can all take care of kids. When you take care of kids, there's an issue of trying to get good delivery of inhaled corticosteroids in the childhood population. So in summary, restriction of access is designed to discourage the use of an excellent drug with optimal patient compliance and no proven toxicity. The alternative choice has a failure rate of 15 to 45%. I'll entertain any questions.

Board Member Kuhls: I want to make two comments, well actually I'll make three. First comment, I think, are you saying that the New England Journal of Medicine's review board is biased or should not, did a very poor job as peer reviewers of their journal article because that study was biased because it was looked at or it was controlled by a pharmaceutical company ... that's what I interpret you as saying.

Dr. Imes: In my opinion, this is a biased study. Now the reason why it's biased .....

Board Member Kuhls: But you said it was because it was looked at by GSK or something like that, so let me, that's fine, but let me say to you, why should I believe anything that says "data provided by Merck"?

Dr. Imes: Oh, well the reason why it's stated "provided by Merck" is it's actually two drug studies put together (unintelligible) . .

Board Member Kuhls: But it's provided by Merck.

Dr. Imes: No . . .

Board Member Kuhls: Just like you said it was looked at by GSK.

Dr. Imes: I agree with you 100%. I mean I'm not trying to tout this as the answer. I'm just saying that when you look at asthma literature in particular, just like you're used to doing, it is very hard to just set down the true facts in every study because each .....

Board Member Kuhls: Including Merck's .....
Dr. Imes: Including Merck's data. I agree 100%.
Board Member Kuhls: Just as long as you realize that most of the asthma research now is looked at by pharmaceutical companies, so you can't, you have to look at the peer reviewers that reviewed the journal article and I think if you're, if you're getting on New England Journal, you're pushing it compared to a lot of the research that I see done by pharmaceutical companies.
Dr. Imes: I agree. Yeah, I was really disappointed because this is a very important .....
Board Member Kuhls: That's a very important study.
Dr. Imes: Yeah. The Asthma Clinical Research Center is a very important network of people to study asthma and I'm very disappointed because what they did, the reason why it was biased, is they selected patients who were responders, good responders to bronchodilator administration. We know from the price study done by Richard Martin up in National Jewish, and some other studies, that those are precisely the patients who have the best inhaled corticosteroid response. So instead of taking all comers which is this study that I showed you here, this is all comers, this is not selective according to their response. They instead chose those that they should have known would be the best inhaled corticosteroid responders. Does that make sense?
Board Member Kuhls: Yeah. No I understand. My second point is the concept that if a medication is restricted by the Health Care Authority or me, Tier 2 or Tier 3, by any other formulary PBM out there, that that means that that drug cannot be used or be used clinically because it's so restrictive. And I'm not so sure that when we restrict drugs here at the Board, that it means that those drugs won't be available for patients that need it, or aren't doing well.
Dr. Imes: Well, that I don't know. But I think it would be an excellent study to do. I think that would be, that's really what you really need to know here. Are these restricting these drugs?
Board Member Kuhls: But I think, I think that's very important, okay? I think that if you don't restrict medications at all, you know, not even care what the medicine is, the way healthcare costs are is that we won't be able to treat anybody without controlling some of the costs. And so you have to look at efficacy and costs, but the concept of restriction automatically means that nobody will be able to be allowed to use Singular no matter what we decide, I think is very unfair. Will you agree with that?
Dr. Imes: I agree with that, yes.
Board Member Kuhls: Okay. My third point which is probably my most uncomfortable point, but all that literature that you gave to me the last time, basically didn't show any studies that showed that in allergic rhinitis that montelukast was any better than inhaled nasal steroids.
Dr. Imes: I didn't say they did.
Board Member Kuhls: Or, when you talk in terms of treatment guidelines and studies and evidence-based medicine, there was nothing in that paper that basically supported the concept of an allergic rhinitis that .....
Dr. Imes: What you asked me for was references. And I gave you references; I did not give you the papers. The references are in the back. You asked for references. I did not have those papers with me but I would be happy to get them for you.
Board Member Kuhls: Okay, because how I remember it, I remember telling you, well you need to give Merck those studies because Merck, you know, I've been looking through their banks and they don't have it, so that's why I was, and I didn't find them when you gave me, and I just wanted to point that out.
Dr. Imes: Yeah, it's in the references. It was not in the actual papers.
Board Member Kuhls: That's all I have.

Materials included in agenda packet; presented by Drs. Le and Keast.

MOTION NO. 1 Dr. Feightner moved to approve as noted below; seconded by Dr. Kuhls.
Option 1 (allergic rhinitis): For members two years of age or older - Trial of an antihistamine and nasal corticosteroid, each 14 days in duration, that has failed to relieve allergic rhinitis symptoms. Agents may be used concomitantly or consecutively within the past 30 days. For members less than two years of age - Trial of an oral antihistamine, 14 days in duration, that has failed to relieve allergic rhinitis symptoms within the past 30 days.
Option 3 (asthma): For members 11 years of age and younger, petitions with a diagnosis of asthma OR claim for inhaled corticosteroid OR three claims for a rescue medication within the past year. For members 12 years of age and older, petitions with a diagnosis of asthma AND a trial of corticosteroid and LAB_2A within the previous six months and a documented reason for trial failure.
ACTION: MOTION CARRIED.

MOTION NO. 2 Dr. Gourley moved to grandfather patients that have a diagnosis of asthma and not grandfather patients with diagnosis of allergic rhinitis; seconded by Dr. Meece.
ACTION: MOTION CARRIED.

AGENDA ITEM NO. 10: **A. VOTE TO UPDATE ANTIDEPRESSANTS PBPA CATEGORY**

B. VOTE TO PRIOR AUTHORIZE PRISTIQ®

For Public Comment, Pauline Patrick: Hi, my name is Pauline Patrick and I'm a pharmacist representing Forest Pharmaceuticals and I'm here today to talk about escitalopram, Lexapro, an SSRI indicated for major depressive disorder and generalized anxiety disorder. There are many new health economics studies available involving escitalopram in major depressive disorder. One study is conducted by Dr. Urder and colleagues which compared treatment adherence of escitalopram to generic SSRI's. They

used a national managed care database and patients that were initiated on escitalopram were 30% more likely to stay on therapy at two months and 42% more likely to stay on therapy at six months, versus patients initiated on a generic SSRI. Another health economic model was conducted by Dr. Woo and colleagues and there they compared the treatment compliance, healthcare costs and resource utilization of escitalopram to other SSRI's and SNRI's in patients with major depressive disorder using another national managed care database. This data showed that escitalopram patients were more likely to be adherent to their antidepressant therapy compared to other SSRI's and SNRI's treated patients. escitalopram initiated patients were 4% less likely to discontinue therapy and 9% less likely to have their medication therapy switched than patients initiated on other SSRI or SNRI. Escitalopram patients also had significantly lower hospitalization days, hospitalization rates and ER visits per 100 patients. In a 6-month analysis of healthcare costs, escitalopram treated patients demonstrated a significantly lower total healthcare cost by $839 per patient. Additionally, a sensitivity analysis conducted on this data which assumed that all other SSRI's and SNRI's were priced at fewer dollars but escitalopram costs remained the same. escitalopram initiated patients still had a $273 lower total healthcare cost per patient. So how did escitalopram, Lexapro, compare to those patients initiated on citalopram, Celexa. Dr. Woo and colleagues compared patients initiated on these two agents using the same national managed care database. In that analysis, patients initiated on escitalopram were significantly less likely to discontinue therapy and were significantly less likely to switch therapy than patients initiated on citalopram. Escitalopram patients also had decreased total healthcare costs with lower hospitalization rates, days and fewer ER visits, compared to patients on citalopram. The packet the College of Pharmacy has provided to you, the drug utilization review of antidepressants, lists several clinical studies comparing escitalopram and citalopram in major depressive disorder. In one of the studies by Moore and colleagues, escitalopram and citalopram were compared in a multicentered double blind randomized 8-week trial and outpatients in this trial were severely ill. They had an average base line MADRS score of 35. The primary outcome measure was a mean change in MADRS total score for baseline. Escitalopram patients did have significantly reduced depressive symptoms over citalopram and this was demonstrated to be statistically significant. Moreover, escitalopram patients had a higher percentage of patients that were responders and a higher percentage that were remitters at endpoint, compared to citalopram. So tolerability was also reported to be better for Escitalopram than citalopram, with twice as many patients withdrawing in the citalopram arm than in the escitalopram arm. So patients demonstrated better tolerability on escitalopram than on citalopram. And contributing to escitalopram's excellent safety profile is the lower incidence of drug-drug interactions, with escitalopram having minimal cytochrome P450 inhibition. Additionally, dosage adjustments are not necessary with patients with mild to moderate renal impairment or in patients with hepatic impairment, which are important for mental health patients in which multiple drug regimens and comorbid elements are a problem. So in conclusion, Lexapro is an effective treatment that is well tolerated for patients with major depressive disorder and generalized anxiety disorder.

Board Member Muchmore: I assume that the studies that you cited that said the cost, overall medical costs were less with people on escitalopram were retrospective studies and not prospective studies?

Dr. Patrick: Yes. They were looking at databases from managed care companies, looking at pharmacy and medical claims and (unintelligible) claims.

Board Member Muchmore: And when you say significantly better, you know you can get significance by just having a large population when the difference is minimal. I don't know what significantly better means. Are you meaning 2% better?

Dr. Patrick: I have percentages, those are one that you were .....

Board Member Muchmore: When you were saying that escitalopram relieved depressive symptoms significantly better and had less .... what was it .....

Board Member Gourley: Hospitalization days, is that .....

Board Member Muchmore: But I, what I'm saying is, what do you mean by significantly? Do you mean 2% did better or 50% better, or what?

Dr. Patrick: Okay. In the data from the managed care database, when we were looking at hospitalization rates, the hospitalization days were 31% lower and emergency room rates were 15% lower in that study of Dr. Woo. And as I mentioned, the discontinuation rates were 4% less and the switching rates were 9% less. So in the matter of time, I didn't include all the percentages, but I would be happy to provide those to you.

For Public Comment, Khalil Saliba, MD: I'm Dr. Khalil Saliba. I'm a psychiatrist in Tulsa and I drove all the way here tonight to share my concern about the fact that we have to, patients have to fail two generic antidepressants before they can be authorized to use a non-generic antidepressant. I'd like to tell you that depression is a major problem in the United States. About 60 or more percent of the general population suffers from major depression. It is one of the top disabling conditions in the country and it carries a suicide rate of about 15%. In other words, 15% of patients who suffer from major depressive disorder commit suicide, or attempt to kill themselves. Furthermore, the remission rates for the treatment of depression are pretty low; 35% to 45% at best, depending on what study you're looking at. In this latest, biggest trial of treatment of major depressing, the STAR*D trial, which I happen to have the chance to participate in, the response rate was about 35%. The APA recommends that we start with an SSRI. Pretty much all SSRI's have equal efficacy in the treatment of major depression; however the guidelines differ when it comes to what do we do next. It's easy to treat or to start treatment of major depression. It's not easy to know what to do next when the first medication trial fails. Now why is this important? Well it's important because the sooner you treat major depression, the better the outcome. The longer it goes untreated, the worse the outcome and the more medications you fail, the harder it becomes to treat. And therefore, the higher the disability rate, the higher the suicide chances, and everything else becomes ..... there's physical symptoms associated with depression that become worse as you let it go. So requiring two generics basically means that you have to use two SSRI's or fail two SSRI's before you either go within a class to a non-generic medication or go to an SNRI. So what's wrong with that? Well, what's wrong with that is that as far as I know, the official oversight from the FDA over knockoff or generic medication production is very poor. In other words, there is not as much oversight as there is for the non-generic medications. So the generic companies are given the latitude of

putting anywhere from 80 to 100% of what they say the pill contains. So 20 mg of Prozac may not actually, fluoxetine, may not contain 20 mg of fluoxetine. It may contain anywhere from 16 to 20. So when you think you're giving the patient 20 mg, you may be giving them 16. And I, basically I'm here to just relate to you my clinical experience which has confirmed that and I have had a lot of patients where I have to go up on the dose because the regular dose which would have otherwise worked, did not work. And my only explanation for that was, you know maybe the dose was not enough. Maybe there wasn't enough medicine in the pill. The other odd problem is that generics depend on what kind of supplier the pharmacy that you're working with is working with. So if patients transfer pharmacies, they're going to transfer generics and the reliability becomes a problem because now they're changing suppliers altogether, so we don't know who is making those pills and we don't know whether those pills are going to work or not, and therefore, they may risk relapse. And I've had many patients relapse because their insurance company insisted that they be tried on the generic, even though they were doing well on their non-generic antidepressant. So those are some of the things. I think that you know, the other thing is, is when you look at the treatment of depression, you can start with whatever you like but then if you fail the first antidepressant and you go to another antidepressant of a generic quality that is similar to the first one; for example you start with fluoxetine and you switch to paroxetine, which is extremely similar in pharmaceutical characteristics to paroxetine, to fluoxetine you're really not doing the patient any favors because you're basically trying the same thing. And that prolongs suffering and prolongs the time to recovery and to remission. So I think requiring a generic as first line, I can understand that given the costs and the times we live in, but I think it's really doing a disservice to our patients to require them to fail a second generic. I think that depression is a very serious condition, it's very disabling and it does justify the cost. The alternative, as you have seen, and as I have seen in my practice, is hospitalization, sometimes it can be prolonged, and sometimes hospitalization or death, at least suicide is the alternative. And I don't think I would or any one of you physicians in this room would be willing to put their patients at risk for that. Thank you.

Board Member Feightner: Just a general comment. I don't think that generic medications are allowed to deviate 20% in active ingredients in the medication. I believe that is not the correct interpretation. I think there's a 20% deviation in a statistical value, and I can't remember what it is off the top of my head. But I just wanted to make that general comment. I don't believe that's the case. An active ingredient cannot vary by 20% among, from generic to brand name, or from generics to generics. I don't believe that is the case.

Board Member Kuhls: Unless you use dig and they double the amount in it….

Dr. Saliba: The problem is that the generic companies are not, you know, their oversight over them is not as stringent as with the non-generics .....

Board Member Feightner: I disagree with that too. I don't think that's right. That's not true.

Dr. Saliba: So what is the explanation for why some patients do better on non-generics and when they're given a generic they completely decompensate?

Board Member Gourley: What did you do about that? When your patient failed? Did you file a report with MedWatch through the FDA and say my patient failed on the generic?

Dr. Saliba: No I put them back on the generic. I never believe in..... if I have a, if I get depressed or I have a loved one who's depressed, I would never put them on generic. That's my belief and that's how .....

Board Member Gourley: Well but you're saying that the FDA's not doing their job, but the only way they're going to do the job is if you do that.

Dr. Saliba: No, no. I didn't say that they're not doing their job. I said that the oversight over non-generics is much more stringent than it is over generics. Because generics, anybody can make them…

Board Member Gourley: I don't believe that.

Board Member Feightner: I don't believe .....

Board Member Feightner: I don't believe that's the case.

Board Member Muchmore: That's not FDA policy. And that's not the way the inspections are carried out. They're very stringent on the generics, and .....

Dr. Saliba: I don't know why then some patients do better on the non-generics and decompensate on generics. Or when they switch pharmacies they completely you know, go .....

Board Member Muchmore: Depression is a disorder that's subject to exacerbations and remissions in the first place and just going by impressions like that really doesn't give you valid information. You want valid information on a drug, you have to do a double blind controlled trial, you count the pills. Because the most common reason for changes or for exacerbation or remission of their condition are failure to take the medication. We have a similar situation in people that have gospel beliefs that certain brands of thyroid are different from other brands. The only thyroid pill that was ever found to be substandard was Synthroid. In 1983 it was found to be 20% less absorbed. The FDA went out to them and said, Synthroid you have to make your pill as good as the generics. Now that's reality. You know, we know for a fact that there is no assurance because somebody put a brand name and a high price on it drug, that it is more likely to contain the right amount or be absorbed as well. It just ain't true.

Board Member Feightner: Or that oversight is less for a generic manufacturer versus a brand manufacturer.

Board Member Muchmore: Despite the fact of Synthroid's track record, we have people who fervently believe that Synthroid is the only thyroid people can take. And we know very well that the reason the people vary is somebody puts them on proton pump inhibitor and their absorption of thyroid drops 30%. The doctor doesn't know that, so he blames it on a generic. They start taking zinc for the colds or something and they fail to absorb the thyroid. You know, there are millions of reasons why people can seem to fail, but we like to blame it on the generic or changing pharmacies.

Dr. Saliba: Well, let me just say, tell you one thing. I'm not blaming on anything. I'm just relating to you my experience. And I am, I feel confident enough to go through all these questions that you have raised with the patient to make sure that they did

not change, they are compliant with the medication. The best is an A-B-A-B trial. So they changed pharmacies or they go from non-generic to generic, they fail. They go back to the generic, they do well. Now they go back to the non-generic, they fail again, or they change pharmacies, they fail. They go back to their old pharmacy, they do well. They're taking their medication, everything remains the same. I absolutely agree with you that yes, the question is a recurring condition, but when you change medications and you see the results right away and then you change back to the old medicine and those conditions subside, or those side effects or decompensation subsides and the patient is doing better again, I don't think that there's any .....

Board Member Feightner: On the brand name, what happens if they're on the brand name and they recide again, you know. Well things go, you went from generic back to brand and they have remission, is it the drug again? Or is it the condition itself has gone down? How do you differentiate a...

Dr. Saliba: decompensate?

Board Member Feightner: ...yeah, decompensate. How do you say that, you know, it's the drug. You can't without a .....

Dr. Saliba: Well when you change drugs, you can never be 100% sure, but when you change drugs and they decompensate, and they decompensate within a period of one or two weeks and then they go back to their original drug and they do well and they continue to do well for several months, now if they decompensate several months down the road, then that's their condition, probably, decompensating. But when they decompensate within two weeks' period from the time they changed medications, that's not, that's not the condition, that's changing the medicine.

Board Member Muchmore: That kind of observation is hypothesis generating, but it's certainly not conclusion delivery, you know. It's hypothesis generating only, and you have to subject something like to trial.

Dr. Saliba: Well, when you do it with patients .....

Board Member Muchmore: That's one of the problems in medicine is there's too many hypotheses to test.

Dr. Saliba: But when you're dealing with patients who have depression and who have risks of suicide, I'm not ready to test anything, at least not in my clinical practice.

Dr. Ron Graham, College of Pharmacy: Doctor, I'll just ask you a question. In recent years, the brand name manufacturers are actually buying generic companies and producing the same generics as their product. So how do you explain why a brand name company like whatever we've got here would go out and buy a generic company in order to make the generics? That right there speaks for itself .....

Dr. Saliba: You know, I'm not speaking for any brand name companies. I don't know how they do it. I don't know what they do.

Dr. Graham: I'm talking about the difference between brand and generic though.

Dr. Saliba: I'm just relating to you my own clinical experience in my own practice. That's all I'm doing. I don't know what the details and when they buy, what do they do, I have no idea.

Board Member Feightner: I think Dorothy (Board Member Gourley) is right in her suggestion, if you strongly feel that there are certain generics out there .....

Board Member Feightner: ..... there are not as effective or don't contain the active, much as active ingredient, MedWatch is the way to go. Find out who it is. Is it Mallinckrodt, is it Teva, who is? Write it up, send it in. And someone there will review it and if you put enough of them together, then the FDA will look at it.

Board Member Gourley: They'll look at one.

Board Member Feightner: Huh?

Board Member Gourley: They'll look at one incident. They'll give you a letter back and say we went to the company, we looked at their quality controls, we looked at whatever.

Board Member Feightner: We tested it.

Board Member Muchmore: And I've done that and they do.

Board Member Gourley: And they'll do it. And they give you a letter back.

Board Member Muchmore: They're very vigilant.

Dr. Saliba: So what do you do in the meantime when the patient is decompensating and they're writing letters and .....

Board Member Gourley: Well, exactly what you did. You did exactly what you wanted to which was go back to a brand name. But you've still not solved the problem by detecting, if you will, your own experience, detected that that drug was inferior. Well if you have, if you want the patient to have a better outcome, then their insurance is telling them they have to do a generic, or whoever else is telling them they have to do generic, so it would be your responsibility to see that the generics are as good. Because you're making them buy a brand name, some people, you know, their insurance won't pay for a brand name, and so you're forcing them into buying a brand name, saying that it was a better drug.

Board Member Feightner: Don't you have other options? Don't you have other options as a physician to choose besides just an SSRI? Do you have other options out there for depression that add on therapy of another drug or something to add on besides switching them to ..... to me, failing that, there wouldn't be, that doesn't seem like the logical choice to go to a brand name. To me, it's switch drugs completely to a different type of drug or add on to that therapy.

Dr. Saliba: Well it depends on how well they do. Like if you have someone on a medication and they don't do well after six weeks, it doesn't matter what you add on. They're not going to do any better. You have to switch. They didn't do well on this medication. Now if there's a partial improvement, then adding on, called augmenting, may have value. But adding on to a medicine that did not work after six weeks .....

Board Member Feightner: How about increasing the dose? Are you increasing the dose?

Dr. Saliba: That's another option.

Board Member Feightner: Are you increasing the dose?

Dr. Saliba: Yeah.

Board Member Feightner: I mean, are you, are you, are you, are you taking a person that's on 10 mgs of fluoxetine, you take a person's on 10 mgs of fluoxetine and they fail, your initial reaction is to switch them to brand name?

Dr. Saliba: No.
Board Member Feightner: You initial reaction is to go to 20?
Dr. Saliba: My initial reaction is to increase the medication.
Board Member Feightner: You increase the medication?
Dr. Saliba: Yes.
Board Member Feightner: You increase the medication?
Dr. Saliba: Yes.
Board Member Feightner: Okay.
Dr. Saliba: I'm talking about patients who are on adequate doses. I'm not talking about patients who are on sub-optimal doses even though Prozac is a non-linear progression medication. The pharmacokinetics of Prozac do not show that if you increase the dose you're going to get a better response rate. That's the pharmacokinetics of Prozac. It's one of the few ones that, increasing from 20 to 40 doesn't mean that you're going to get a better response. Actually the studies show that there's no better response. We still do it in practice because the studies are one thing, clinical practice may be different. And some patients do improve. These are not the patients I'm talking about. I'm talking about the patients who fail one generic and need to transfer to another generic.
Board Member Feightner: My last point is, you have other options in the meantime to choose, as a practitioner, besides going back to the brand name.
Dr. Graham: You don't have to fail two anyway.
Dr. Gourley: We're not even evaluating this criteria.
Board Chairman McNeill: With that comment, let me bring this discussion to a close. Dr. Saliba, thank you very much. The issue here, let me just say that this issue of generics may have seemed to some to have been tangential, but it is on point as we move forward, because there are generic and brands we will be discussing, so that's why I think it was important to hear that discussion. Dr. Seymour.
For Public Comment, Susie Seymour: Hi, my name is Susie Seymour and I'm a consumer. Just a little background. The problem that I have with some of the medications is that for one, I'm on fifteen different ones. So trying to find the right medication is interesting. Not only am I on psych meds, but I'm also on meds for my fibromyalgia, my osteoporosis, and my neuropathy. And I have a whole other list that I'm not going to go into that, okay? So the problem is, is that before I found the right cocktail I was what you would call a frequent flyer at fire stations. Do you guys know how that happened? How you know when you become a frequent flyer is when they already know what medications you're on. Okay, for one, because I didn't have the right medication, it was like medication such as for my lupus, fibromyalgia and also for my depression. And it took me six years to try to find the right medication, unfortunately. And a lot of it has to do with, I've tried I couldn't tell you how many medications on this list that I've tried. And I've failed. And if today I'm working, I'm planning to go back to school. I'm holding down a job. I'm living independently. I'm being a productive citizen, and I'm not laying on the floor being hysterical, having muscle spasms where I can't move. But if I had to go back and try some of the medications that I've already known that's failed that I couldn't function on before, you know. Depending on how long I'd have to try it, I might lose my job, I might lose my housing. I definitely probably wouldn't be able to go back to school. I would lose all function if I had to go back to some of these medications that I've already tried. Which to me is just kind of going backwards, when I've fought so hard to get where I'm at now. And so I'm just definitely here to let you guys know that, you know, medications do help. That having the right medication and having, if I fail, which probably will happen, because most medications you grow dependencies on or tolerance to, so you have to find another medication. If I have to go back, am I going to end up losing my job? Am I going to end up losing my house? Because what is it, four to six weeks before you can find out some medications you're taking are appropriate or not? You know what I'm saying? So that's kind of sort of where I'm at. I'm also a mental health advocate. When I hear all these stories about, you know, well that one worked, but that one didn't work, you know? And the doctor's not listening to me that that one worked, but my insurance no longer covers that one. So now I have to change it. You know? Unfortunately when you get on the right cocktail, and I do call it a cocktail because it also includes your lifestyle such as your diet and your exercise, it includes everything. It's no different than being diabetic, or having heart disease, you know? Which a lot of people have stigma, but that's a whole other issue. That when you find the right cocktail, you know, you can do amazing things and actually start participating in life and start contributing back to society. But if you don't have the right cocktail or something in your cocktail gets changed, you get back on that vicious cycle. I personally don't want to become a frequent flyer to the firefighters in my neighborhood again. I don't mind going and seeing them, I don't mind baking them cookies, but I prefer only to see them there and not at my house because I'm having anxiety or some other issue. I also don't like going to the ER. I've been there way too many times. I don't want to go back. You know? When I broke my foot, it took me my mother to convince me several hours that it was OK to go to the hospital because I'd been there so many times because of anxiety attacks that the nurses and doctors were starting to look at me like I was crazy. Well, OK yes. I had a mental health issue, but being treated differently because I have a mental health issue is something beyond that. I like the way I feel now. I like being productive. I don't want to have to go two months possibly backwards because I can't afford it.
Board Member Kuhls: So can I just ask a question?
Ms. Seymour: Yeah, go ahead.
Board Member Kuhls: So what you're saying to me, what I'm hearing is when you find the right medicine, the last thing you want to do is to switch?
Ms. Seymour: Exactly.
Board Member Kuhls: I respect that.
Ms. Seymour: Exactly. And you don't want anything to mess with it. You don't want to really change your diet, you, like, you're starting to pay attention, OK, what am I doing? You know, am I exercising, da-da-da-da.

Board Member Kuhls: I respect that.
Ms. Seymour: The sad part is, is for some happen it fails, which, you know, I know that medications will fail. I'm going to have to change eventually, because that's just how your body works sometimes. I don't want to have to go back and try all the drugs and go through six years again of what I went through to try to find another set of medications.
Board Member Kuhls: I respect that, but at the same time, if we knew which one you would respond to the next time, then there wouldn't be any question. The problem is finding the next medication.
Ms. Seymour: But if I've already tried the medications . . .
Board Member Kuhls: But you see what I'm saying?
Ms. Seymour: . . . and they've failed, why do I have to try them again? That's my question.
Board Member Muchmore: That's not even at issue here. The issue is initiating therapy, not somebody's who's stabilized on a therapy that's working well for them.
Board Member Kuhls: That's not what the issues are here.
Ms. Seymour: What I'm saying, though is if I've failed and I'm like on a different tier, 'cause you guys have tiers, right? But I'm on like a tier 2 or 3 and I fail, would I have to go back to tier 1?
(multiple responses): No. No.
Ms. Seymour: I've had doctors tell me that I have to re-try medications and it gets really interesting when I fill medications and I have to get prior authorizations.
Board Member Feightner: There's certain pharmacy benefit manager companies that have that requirement, okay? You don't have that within this, in this criteria.
Board Member Muchmore: We tend to grandfather somebody stable on a drug.
Ms. Seymour: That's fabulous and I totally get that. The problem is is I've seen people, like when I started getting mental health services, there's actually money in DMH funds, Department of Mental Health fund, so when I absolutely had nothing, I could get services. Only a couple of years went by and they depleted the services, so the people that needed the same services that I got two years ago because they ran out of funds were no longer able to get those services. And I deal with people all the time who are just coming in, finding the right medication, and trying to find the right medication, and are stuck trying the same medications over and over again.
Board Member Feightner: We, we don't typically do that. That's not, not, I guess this is the wrong DUR Board I guess to come to and that. I'm glad you found your cocktail and I wish every practitioner could day one, tell you what that magic, not have to put you through six years of that. I wish they knew that, but that's not the case.
Ms. Seymour: Well, you know that's a whole bonding experience, growing experience, you know. I don't have a problem with that. I just don't want to have to go back. And there's, I've witnessed people having to go back, like a co-worker of mine. They were prescribed a certain medication and they had to take two or three months off because of they couldn't get the medication that they needed.
Board Member Feightner: Your point is taken. Your point is definitely taken.
Board Chairman McNeill: Thank you.
Ms. Seymour: Thank you.
Board Chairman McNeill: Would the Board like a 10-minute break or would it be agreeable to you that if you need to go, just go. Would that be fine? Okay, we're going to move on.
For Public Comment, Dr. Art Rousseau: Let me introduce myself. I am Dr. Art Rousseau. I'm a psychiatrist in private practice here in Oklahoma City. I'm also a clinical professor at the University of Oklahoma Health Sciences Center. Today I'm here as the chairman of the public information/public affairs legislative committee of the Oklahoma Psychiatric Physicians Association. I've been asked to speak to you on behalf of over 260 psychiatrists who are members of the OPPA. I appreciate you letting me take a few minutes to address the subject of adding a third tier to medication formulary for antidepressants. We as psychiatric physicians believe this proposal is of concern to the health and welfare of the mental health community which we serve. I understand that you have a responsibility to create savings and control costs for the Oklahoma Health Care Authority and the drug utilization and Medicaid population in Oklahoma and I commend you for your volunteer service and your staff for working on behalf of our State. However, we as psychiatric physicians, have a concern anytime there are obstacles placed between the treatment of our patients and our patients receiving the most effective prescription, especially in the mental health area. Adding a third tier to the product based prior authorization program could have negative consequences in patients since they may have to fail on two or more different drugs before they get to the one physician may clinically assess as being the best medication to prescribe for the patient. As all physicians, we believe that when needed, access to the best medication for the patient is one of the most important issues in treatment and that any program that requires more steps to be followed to find that drug, especially if that program is not based on clinical but financial issues. This will only increase pressure on the Department of Mental Health and Substance Abuse as we will have more noncompliance and subsequent treatment failure on medications. Remember, in patients who are on psychotropic medications such as antidepressants, treatment failure will lead to increased medical costs through increased outpatient visits and possible hospitalization. This would be reflected in significant increases in the overall cost of psychiatric treatment care. More importantly, treatment failure in this patient population can result in increased morbidity and mortality rates and attempted and completed suicides. Overall medical costs increase due to medical treatments such as ICU admissions and surgical care that are necessary when suicide attempt has occurred. Now it is our understanding that the Board has discussed the possibility of exempting psychiatrists from this proposal. As psychiatric physicians, we appreciate the trust you are placing in our expertise in discerning appropriate medication treatments, but it is well known that non-psychiatric physicians such as internists, family physicians, gynecologists and pediatricians also prescribe antidepressants and are very competent in discerning appropriate medication for their patients. As I'm sure you are aware, there is very little chance that only psychiatrists would see all of the patients needing mental health care. We ask you to think

long and hard about this decision and will affect our very delicate and vulnerable group of patients, the mentally ill of Oklahoma. Now knowing that the Department of Mental Health and Substance Abuse would be greatly affected by your proposal, specifically by providing care for the treatment failures, the Oklahoma Psychiatric Physicians Association is greatly interested in their opinion regarding this proposal and asked that they be directly involved in this decision process so that they may provide you with information regarding the medical and financial impact this decision will have. Thank you very much. If you have any questions, I'd be happy to respond to them.

Board Member Kuhls: I understand everything you say. But I think you're talking in front of the wrong people. I think what you should do is talk to all the pharmaceutical companies that are Tier 3 and tell the pharmaceutical companies in Tier 3 that you need to give the State of Oklahoma and the people who have mental illness in the State of Oklahoma and the people who have depression in the State of Oklahoma a rebate to the taxpayers so that they can move their drug to the Tier 2. I don't know if you totally understand this three class system. This three class system is to try to get all the drugs that are Tier 3 into Tier 2.

Dr. Rousseau: Let me say, I really don't know how to respond to that. I'm not involved with any pharmaceutical company. I am coming from a clinical position as a physician. I look at that Tier 1, Tier 2, Tier 3 proposal and it is not good medicine. Now that's all I can tell you from a clinical standpoint.

Board Member Kuhls: Well right now, when you look at the proposal, there's Tier 3's but there's nothing in Tier 2. There right now is only a 2-tier system.

Dr. Rousseau: Right.

Board Member Kuhls: And so that if there's no pharmaceutical companies that want to place their drug into Tier 2, there'll be a 2-tier system.

Dr. Rousseau: Our patients are the ones that fail.

Board Member Kuhls: There will be a 2-tier system.

Dr. Rousseau: Oh, okay. Well I guess that's a very good point. So I guess if all pharmaceutical companies choose to .....

Board Member Kuhls: So if all the pharmaceutical companies decide that they don't want to be a supplemental rebated thing and don't want to go to Tier 2, if all of those say we don't want to participate, you will have your Tier 2 system. But if one of those pharmaceutical companies want to give a supplemental rebate in which the committee here, we're not even involved here in the DUR Board, but the people that are on the committee for supplemental rebates, if one of these companies can give a good response, and who knows what that is, then that's their, that's their ..... ability to do that.

Dr. Rousseau: Well if I could respond to that. Number one, I feel like I am talking to the correct committee. I think you're talking to the wrong person as to how to solve the problem of what the pharmaceutical companies need to do. That's what you, no, you need to talk to them if they're going to do that.

Board Member Kuhls: Well, that's .....

Dr. Rousseau: But I'm telling you the way this is set up .....

Board Member Kuhls: Well, that's the purpose. The purpose of this tier system is to try to deliver to the pharmaceutical companies a method where they all the, I hope that every one of these Tier 3 drugs, okay? I hope that every one of these move to Tier 2.

Dr. Rousseau: And if they don't it is at the cost of the mentally ill of Oklahoma and that is my concern and that should be your concern.

Board Member Kuhls: And that is my concern. That's why I think it's important that the pharmaceutical companies move their drugs all to Tier 2.

Dr. Rousseau: Now all I want to say is, looking at the way it's set up right now, even the way it's set up, this is giving psychiatrists very few options outside of generic SSRI's. And I don't have a problem with that. I'm not going to get into the issue that was talked about earlier. I think that's not an issue. You know, I use the generics, that's not the problem. When I look at how this is set up, if I move out of that SSRI's and try to get a dual acting antidepressant, I can't tell you when the last time was I Effexor. The side effect profile of that is terrible. That's why they made Effexor XR. Venlafxine, Effexor, you're not talking about Effexor XR. You've got it over here in Tier 3.

Board Member Kuhls: That's why we're hoping, okay?

Dr. Rousseau: At the, okay. At the cost of the mentally ill of Oklahoma. I cannot respond to what the pharmacies ..... companies can do.

Board Member Kuhls: I'm not sure it's at the cost of the DUR Board, but I think maybe some of these prices that are occurring and so on are at the cost of .....

Dr. Rousseau: You should be representing the mentally ill in this, in this topic .....

Board Member Kuhls: I actually am trying, because I'm hoping that if we go through with this system that there will be only a Tier 2 system because everything will be moved to Tier 2.

Dr. Rousseau: Well I think that, that it could fail miserably at the cost of the mentally ill. And that's why I'd asked you to think long and hard about trying to initiate something like this.

Board Member Rhymer: I don't think all the mentally ill in Oklahoma are on this program either, so, I don't know what the percentages is, but .....

Board Member Bell: A great many of them.

Dr. Rousseau: No of course not.

Board Member Rhymer: There are a lot, but .....

Board Member Kuhls: There are a lot.

Dr. Rousseau: Again, I'm not trying to respond to every mentally ill patient in Oklahoma, but certainly the people that are on, in this program that would have to deal with this are the people that you're representing.

Board Member Kuhls: Because I would like to see a reduction in pharmaceutical costs so that those extra dollars that are saved can go to service, or .....
Dr. Rousseau: No argument.
Board Member Kuhls: Then I think we agree.
Dr. Rousseau: But what we disagree on is how you're going about doing it, and it's going to be at the cost of patients and it is patient lives.
Board Member Kuhls: We have been successful in many other drug categories of using the supplemental rebate program to help with other patients with other diseases. It's not like this is a brand .....
Dr. Rousseau: Alright, I think this is really a unique situation.
Board Member Kuhls: It's not like this is a brand new scheme, okay, that has never been used by this committee, okay, this tier system and moving to Tier 2. We've been using that for other classes of drugs with people with very serious diseases and it seems to work. And so really, I think, I'm hoping that you may be, it may be that nobody, no pharmaceutical company moves to Tier 2. Then there's a 2-tier system. Or everybody moves to Tier 2 and then there's a 2-tier system. I'm hoping that one of those happens.
Dr. Rousseau: I would hope that they would all go down and cut their cost by 100%.
Board Member Kuhls: Wouldn't that be great? Wouldn't that be great? Wouldn't that be great?
Dr. Rousseau: That would be great, but I don't .....
Board Member Kuhls: That's probably not going to happen, right? There's going to be some that will probably move and some that won't.
Dr. Rousseau: And then that will affect my clinical judgment.
Board Member Kuhls: And hopefully Effexor ER, you know, I don't use these drugs a lot, but hopefully, Effexor ER will be one of those to go to Tier 2.
Dr. Rousseau: Well, the thing is, you're, you've got in Tier 1, Effexor that I don't know a psychiatrist that uses that unless they just don't have any other option because of a program like this.
Board Member Kuhls: That's why I think that a lot of discussion has to be with the pharmaceutical companies to move these drugs to Tier 2, and I think and I really feel strongly, that you and your group needs to participate in that. I hope that you guys work with the Board to try to get better services for mental health, to reduce some of the medication costs, okay? I hope you work with, I hope, well I .....
Dr. Rousseau: You're preaching to the choir. I mean, that's why I'm here.
Board Member Kuhls: But what I'm trying, but what I'm trying to say is .....
Dr. Rousseau: That's why I've been here since 5:45.
Board Member Kuhls: I understand, but what I'm trying to say is and what you need to listen is, this Board feels the same way that you are, we're all here for the same goal.
Dr. Rousseau: We're just differing on, right. But we're differing on how you're approaching doing it and that cost is going to be
Board Member Gourley: We don't have any other tools.
Board Member Kuhls: But I haven't heard of a method for you that you've given us the reduced costs with a 2-tier system.
Dr. Rousseau: Well if you'd like me to come up one ..... I don't know if I could.
Board Member Kuhls: Well that's what, if you have ....
Dr. Rousseau: But I don't think this is the answer.
Board Member Kuhls: If you have a, if you have a Tier 2 system that will reduce costs, we would love to hear it.
Dr. Rousseau: Well, the Tier 2 system I think has been working to a certain extent. And the fact that you would use a fluoxetine or citalopram is a wonderful attempt at trying it. But when you start going into the way you set up your tier system, is that is if I have to move out of that SSRI, I'm moving to SNRI's, then you're giving me no choice of really having a good shot at getting this patient to comply with the medication and respond. And if they don't they're going to end up in the ER, whether they're in there with a bullet in their head, or with an overdose, and you're going to see them in the ICU unit, and you're going to see them in surgery. And that is going to bump the cost way up.
Board Member Kuhls: But we haven't even seen what happens in Tier 2 yet, okay. The Tier 2 system, we don't know how that's going to fall out yet.
Dr. Rousseau: Okay, and you're telling me that you, now why are you even trying to introduce a Tier 3? (unintelligible)
Board Member Kuhls: No we're not introducing a Tier 3. The Tier 3 is already there. We're trying to move to get a Tier 2 system.
Dr. Rousseau: The Tier 3 system is already there?
Board Member Kuhls: We have a 2-tier system. We're trying to make a middle tier, okay.
Dr. Rousseau: I understand.
Board Member Kuhls: We're not trying to add a third or a farther out tier.
Dr. Rousseau: Well, you're ending up with the same situation. You're having three tiers.
Board Member Kuhls: Well it depends on what happens in that tier system.
Board Chairman McNeill: Well I think we're, I think you gentlemen are discussing the same point. I appreciate it and I think that hopefully your expertise will come into play as we move forward on this.
Dr. Rousseau: Thank you for your time.
Board Chairman McNeill: Thank you, sir. Dr. Dennis, our last speaker ..... Dr. Dennis. Leland Dennis.
For Public Comment, Dr. Leland Dennis: Mr. Chairman, I'll give you these and you can pass those out now or afterwards, or in between. Hi, I'm Leland Dennis. Can you hear me? I'm a psychiatrist. I'm an investigator. I do clinical trials as well as primarily taking care of patients. I've had that privilege since last century. It's an incredibly exciting time to be a shrink. Last century was

my very first completed suicide in a patient. And those of you that have had that experience know how badly it feels. Using nortriptyline, successful overdose. The SRI's came out and we were told that these were ineffective medicines because they didn't cover all the neurotransmitters. And now they're first line choice. You'd have to choke on the bottle to kill yourself with a bottle of fluoxetine, right? Very safe drug. As Dr. Saliba pointed out, probably the most important piece of literature in this century regarding depression was the the STAR*D. It was a fascinating article. As was pointed out, we psychiatrists do an equally crummy job when compared to our internists, when compared to our friends in family practice, at treating such a powerful disease. And we've heard how powerful it is from the patient. We've heard how powerful from a perspective of a provider. We know that longer trials are necessary. The expectation of a 4-week trial being an adequate trial in any dose is insane. Okay? So saying that somebody failed in four weeks on a trial of fluoxetine, when we know the STAR*D said that a third of people remit at twelve weeks, forces people to change medications prematurely. That drives up your cost, that drives up your morbidity and your mortality. I can't tell you how discriminating the patients are that come to see me. I've tried that, I've tried that, I've tried that, I've tried that, and when I ask them dose and duration, they don't have a clue. So when you look at solutions, I'm appalled by what I, the discussion I just heard. I am absolutely appalled by some of the statements, and I won't go into that. Our goal in treatment is remission. Depression is an illness that's suffered by an entire family. My high blood pressure is my disease. You don't know I have it until I told you. But if I'm depressed, if I have decreased productivity, it hurts everybody around me. Look at presenteeism costs. Look at the problems associated with restricting access to effective treatments. The STAR*D said that we start out with a funnel of people and we add treatments. We augment as Dr. Saliba said. And we get more people and we change and we do all sorts of things and try to make sense of it. And the FDA, excuse me, the NIMH saw such a powerful in combination therapies that they're now funding the ASCEND trial. Starting people with first episode depressions on an antidepressant and an atypical antipsychotic. Can you imagine the cost of doing that? When we have very effective treatments now. When we have very good treatments. We have a drug in your packet. It's from Oregon Health and Sciences Center and it's from 2006. And the data started in April and went backwards. In 2004, duloxetine was approved for major depression. Quickly. An expedited approval for the treatment of painful polyneuropathies and diabetes. In February of '07, a GAD indication. That's not in your packet. How often do you see anxiety in depression in the same individual? Only 60% of the time. Now as an investigator, it's hard for me to enroll people in placebo controlled randomized clinical trials because the criteria is so narrow. It doesn't look like the people walking in. My real life patients come with different degrees of illness. And that's my responsibility as a provider, as a doctor, as a physician, to help that patient make logical and good choices. What I'm being asked to do is fail people on treatments, and two weeks ago when one of the people very close to me lost a husband to suicide, it brought back the memories of those people that have been inadequately treated. And he didn't need to die. Restricting access in this population to manipulate a company to change a pricing structure, I think, is unconscionable. I'd prepared other statements, they've been made by other people. I'll appreciate your time at this point.

Board Chairman McNeill: Comments?

Board Member Kuhls: Was that a person on trial that committed suicide, is that what you're saying, last week?

Dr. Dennis: A person receiving inadequate treatment, yes sir.

Board Member Kuhls: Like, yeah. I think that's part of the problem. This doesn't have to do with this conversation, but that's a problem with the way the government has set up approvals or medications. They should be compared to baselines compared to placebos which is in a lot of the antidepressant studies that are required by the government, correct?

Dr. Dennis: I'm sorry, I didn't quite . . .

Board Member Kuhls: What I'm saying is a lot of the trials to get drugs approved are placebo-controlled?

Dr. Dennis: Yes.

Board Member Kuhls: And unfortunately that puts a lot of patients at risk.

Dr. Dennis: Well, yeah. If you look at, if you wanted to look at study design, the FDA is now seeing suicide as an adverse event of special interest and ..... isn't that a clever way of saying it? It's an adverse event. Yeah.

Board Member Kuhls: I'm just saying, in general it would be awesome to start getting more and more comparative studies to try to dissect things out instead of having placebo-controlled trials to get a drug approved so you can't effectively compare and contrast .....

Dr. Dennis: But as you're fond of saying, sir, I don't think this is the right audience to create those kind of (unintelligible).

Board Member Kuhls: It would be nice, wouldn't it?

Board Chairman McNeill: Any other comments? I would say though, your reference to a comment made about approaching drug companies and costs and how this whole system works being unconscionable, I hope you understand that we deal with 450,000 people in this program, not just the mentally ill. And there is a pot of money that needs to be dispersed. Some of these illnesses are horrendous, non-psychiatric illnesses and it's not just the mentally ill we have to deal with. And in addition to patients, we have to answer to a budget and taxpayers. So I appreciate your comments, but I want you to know that.

Dr. Dennis: Thank you.

Board Member Gourley: Just one more comment about what you made reference to about a 4-week trial. I think what we were trying to do with that criteria was to give you some leeway. We never said you had to change at four weeks. We never said that. We said that was the maximum amount that you had to try before you could change. Now you as a psychiatrist are, as a professional, have said that you might want to treat for six weeks, or eight weeks, or whatever. Well you're free to do that.

Dr. Dennis: And I think that my point on that is this is an opportunity to help educate. And by setting the bar that low, teaches people you don't really have to give an (unintelligible).

Board Member Gourley: I would agree with that.

Board Chairman McNeill: Thank you. Before we move on to Dr. Le's presentation or further discussion by the Board, I'd like to read a letter that came in today from Commissioner Terri White so everybody understands her position. She could not be here tonight. *"Dear Chairman McNeill: The agenda for the Drug Utilization Board meeting on Wednesday, July 9th includes possible*

action on an item than can influence the care provided to Oklahomans receiving pharmacological treatment through our network of community mental health centers. I am writing to request that the DUR table action on Agenda Item Number 10 [Vote to Update Antidepressants PBPA Category and Vote to Prior Authorize Pristiq]. SoonerCare is the pay source for thousands of Oklahomans receiving treatment for mental illness through our agency's provider network. Many consumers use antidepressant therapy as an important tool in support of their recovery. As Commissioner of the Oklahoma Department of Mental Health and Substance Abuse Services, I am asking for additional time to allow our agency's medical director and his clinical staff to evaluate the possible impacts of this proposed change. Sincerely, Terri White, Commissioner".

Materials included in agenda packet; presented by Dr. Le. Dr. Bell expressed concerns regarding approval criteria for children/adolescents, geriatrics, and adult psychiatry. Discussion was held regarding supplemental rebates and drug classes.

10A: Vote to Update Antidepressants PBPA Category

Dr. Bell moved to table; seconded by Dr. Kuhls.

ACTION: MOTION CARRIED.

10B: Vote to Prior Authorize Pristiq

Dr. Muchmore moved to approve; seconded by Dr. Bell.

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 11: 30-DAY NOTICE TO PRIOR AUTHORIZE VOLTAREN® GEL

For Public Comment, James Lieurance: I think I saw more fireworks in this room on both sides of this equation than I saw on the Fourth of July, so if we've established anything this evening, it's that healthcare isn't easy, but I do appreciate the discussion. You have to keep things fairly straight and fairly simple on Voltaren gel this evening. I'm going to review an article that was published by the Arthritis Society and it was published on the launch of this by Dr. Roy Altman, and then after that I'll put forward some ideas before the Board for their consideration. The FDA recently approved Voltaren gel as the first prescription skin gel to treat osteoarthritis pain. The gel contains diclofenac sodium, an NSAID that is the main ingredient in Voltaren pills. *"A prescription topical NSAID is great news for selected people with arthritis", says Roy Altman, professor of medicine in the division of rheumatology and immunology at the University of California (UCLA). "Voltaren gel may be a good option if: You have arthritis in smaller joints. The new Voltaren Gel gives patients the ability to apply something topically, which will not significantly elevate blood levels, but will penetrate the skin and help reduce pain." Going on, "Voltaren Gel works as well as its oral predecessor when it comes to joints that are closer to the surface, such as the hands, knees, elbows and ankles. In the studies that led to the new gel's approval, pain levels fell by 46 percent among people with hand OA after they applied the gel for six weeks. In a 12-week study of people with knee OA, there was a 51-percent reduction in pain",* which I can personally attest to because I have secondary OA of my right knee. *"If you're older than 65, A lot of elderly patients can't take oral NSAIDs because they have stomach or heart risk factors, and they can't take narcotic analgesics because they could become drowsy, could fall and break a bone. You want to avoid pills. Some people with OA who want to avoid systemic side effects and they seek compounding pharmacies so that they can have their favorite painkiller made into a topical formula. Pharmacists literally can take these medications out of the capsule and make them into a gel. This can be fairly expensive, however, and it can be inconsistent from one batch to another. The new gel is less expensive and more consistent than a compounded topical formula. In addition, it comes with disposable dosing strips that show you exactly how much gel to use. You squeeze the gel onto the card and the appropriate the line for your dose, then wipe the card directly onto the joint and rub it gently. Voltaren gel may not be a good option if you are already on an oral NSAID. It's not that the gel's active ingredient doesn't get into your bloodstream – it does. So when some gets absorbed, just substantially less than with a pill. Specifically, 94 percent less is absorbed from the Voltaren gel than from its oral counterpart. However, the new gel should not be used in combination with oral NSAIDs or aspirin because of the potential for adverse effects. When used alone, the only real side effects of the topical products are skin reactions where they are applied. When you have several affected joints. Voltaren gel works fairly quickly – within a week – but let's be honest, the pill works quicker," says Dr. Altman. "And taking a pill would be a lot easier for someone who has multiple joints affected by arthritis."* What I put forth to the Board is, I don't know your risk with GI bleeds. I know the related medical costs that they suffer in Missouri. Missouri reviewed the product, put the product on without prior authorization or restriction because they felt that there was a medical cost savings and a safety issue to the patient that the gel presented. It was interesting that we had the tiering conversation here because we're in a position here, we have a patient where if they're on the generic NSAID it makes no sense to use a gel. And I really as a manufacturer, don't want them used in combination because that does present some safety risk and quite frankly, I don't want the GI bleeds associated with our product. So what I would propose is first line therapy, a 5-tube quantity limit, which would protect any overutilization of the product, no concomitant use with other NSAID's or COX-2's and that this gets kicked over to the PDL committee for supplemental rebate consideration. Other than that, I'm open to answer any questions that you may have.

Board Chairman McNeill: I certainly appreciate your comments.

Mr. Lieurance: Thank you.

Board Member Muchmore: I should point out that the biggest cost and problem with NSAID's is not GI bleeds, but renal failure. You know, we have a population who's increasingly diabetic and hypertensive and they could have a nice creatinine of 1.2 and take a few Advils or something and their creatinine's up to 4 and they put on 30 pounds and come into the ER with pulmonary edema. It is a real problem. I have no idea if this solves that problem. I'm really unfamiliar with it.

Board Chairman McNeill: Do you know?

Mr. Lieurance: Unfortunately in our labeling, we have the same class effect as all the NSAID's, but when you look at the average systemic rate of absorption, it's 6%. We do have edema in our labeling, but that's class effect.

Board Member Muchmore: It would be really interesting to see a study that said, you know, that followed renal function, GFR, because you could really have a point with the gel if it obviated that problem of renal failure that stops so many of our patients from using an NSAID. Now I have no idea what it costs, I've never seen any studies on it. I'm just pointing that out, that that's a major issue to those of us who treat diabetes and hypertension.
Board Chairman McNeill: And a similar product although a very different delivery, Flector patches, is another topical NSAID. Where do we .....
Dr. Keast: It's a Tier 2.
Board Chairman McNeill: It's a Tier 2? Alright.
Materials included in agenda packet; presented by Dr. Patel.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 12: **30-DAY NOTICE TO PRIOR AUTHORIZE LUVOX CR®**
Materials included in agenda packet; presented by Dr. Le.
ACTION: NONE REQUIRED.

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

AGENDA ITEM NO. 14: **FUTURE BUSINESS**
Materials included in agenda packet; submitted by Dr. Graham.
14A: Oral Antifungals Review
14B: Qualaquin® Annual Review
14C: ESA Review
14D: Glaucoma Intervention Report
14E: Hemophilia Review
14F: New Product Reviews
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 15: **ADJOURNMENT**
The meeting was adjourned at 9:20 p.m.

The University of Oklahoma College of Pharmacy

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

Memorandum

Date: July 10, 2008

To: Nancy Nesser, Pharm.D., J.D.
Pharmacy Director
Oklahoma Health Care Authority

From: Shellie Keast, Pharm.D., M.S.
Drug Utilization Review Manager
Pharmacy Management Consultants

Subject: DUR Board Recommendations from Meeting of July 9, 2008

Recommendation 1: Vote to Prior Authorize Osteoporosis Medications

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends adding the Osteoporosis Medications to the Product Based Prior Authorization Program with the following Tiers and criteria.

Tier 1*	Tier 2	Tier 3
Alendronate (Fosamax®) Calcium + Vitamin D†	Alendronate + D (Fosamax®+D) Ibandronate (Boniva®) Risedronate (Actonel®)	Zoledronic acid (Reclast®) Teriparatide (Forteo®)

*Branded products will require a brand name override. Calcitonin and raloxifene are not included as Tier 1 trials.
†Must be used at recommended doses in conjunction with Tier 1 bisphosphonate for trial to be accepted unless member has a recent laboratory result showing adequate Vitamin D or member is unable to tolerate calcium. OTC Calcium and Vitamin D are only covered for members with osteoporosis.

Recommended Criteria for Moving to Higher Tiers:

1. Treatment failure with all lower tiered products, or
2. Contraindication to all lower tiered products, or
3. Allergic reaction to all lowered tiered products, or
4. Specific indication not covered by a lower tiered product.
5. No concomitant use of bisphosphonate therapy will be approved. No additional bisphosphonate may be approved for 365 days following zoledronic acid infusion.
6. Clinical Exceptions:
   a. Risedronate may be approved for members with high risk for gastric side effects.

b. Zoledronic acid will be exempt from prior authorization for a diagnosis of Paget's disease or for osteoporosis if secondary diagnosis meets criteria below.
c. Teriparatide may be used after a minimum 12 month trial with a bisphosphonate plus adequate calcium and vitamin D (unless contraindicated, intolerant, or allergic) and a BMD (T-score at or below -2.5) test within the last month.

Reclast® will be covered for postmenopausal osteoporosis in women who have the following secondary diagnoses:

- Severe esophageal disease (e.g., ulcerations, strictures): ICD-9 codes 530.0, 530.20-530.21, 530.3 and 710.1.
- Inability to take anything by mouth: ICD-9 codes 530.87, V44.1, V45.72 and V45.75.
- Inability to sit or stand for prolonged periods: ICD-9 code V49.84.
- Inability to take an oral bisphosphonate for other special medical circumstances that justify the method of administration: ICD-9 codes 995.29 and V12.79.

Recommendation 2: Vote to Prior Authorize Topical Antibiotics

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends creating a prior authorization category for this group of medications with the following tier structure and criteria:

Tier 1*	Tier 2	Tier 3
Mupirocin Oint 2% Gentamicin Oint 0.1% Gentamicin Cream 0.1% Gentamicin Powder Cortisporin® Oint 1%† Cortisporin® Cream 0.5%†	Supplemental Rebated Tier 3	Bactroban® Cream 2% Bactroban® Nasal Ointment 2% Centany® Kit 2% Altabax® Oint 1%

*Branded products will require a Brand Name Override when generic versions are available.
†Products will remain Tier 1 as long as federal rebate does not change.

Criteria:

- A 5-day trial of a Tier 1 medication within the last month is required before a Tier 2 medication can be approved.
- Member must have a 5-day trial with a Tier 1 and a Tier 2 medication prior to receiving authorization for a Tier 3 medication.
- Clinical exception includes adverse effects with all lowered tiered drugs or unique indication not covered by lower tiered drugs.
- Prior authorization will be for 10 days.

Recommendation 3: Vote to Prior Authorize Auralgan™

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends prior authorization of this product with approval after failed trials of an available generic product containing benzocaine/antipyrine/glycerin, and two (2) trials of oral pain relievers for a duration of 360 days.

Recommendation 4: Vote to Prior Authorize Plavix® 300 mg

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends prior authorization of Plavix® 300mg. Approval Criteria is as follows:

- FDA approved diagnosis of non-ST-segment elevated acute coronary syndrome or ST segment elevated acute myocardial infarction.
- Approval will be for only one dose of 300mg.

Recommendation 5: Vote to Prior Authorize Singulair®

MOTION CARRIED by unanimous approval.

For members with a diagnosis of asthma the following criteria will apply:

Children age 11 and under:

- Diagnosis of asthma OR
- A claim for inhaled corticosteroid OR
- Use of 3 or more rescue medications
- All claims should be within the member's previous year's history.

Children age 12 and older and adults:

- Diagnosis of mild or moderate persistent asthma, and/or exercise induced asthma AND
- Trial of inhaled corticosteroid AND corticosteroid/LAB_2A therapy within the previous 6 months and reason for trial failure.

Edits will be put in place to automatically detect asthma diagnoses and claim criteria and generate AutoPAs where possible.

For members with a diagnosis of allergic rhinitis the following criteria will apply:

- For members 2 years of age or older - Trial of an antihistamine and nasal corticosteroid, each 14 days in duration, that has failed to relieve allergic rhinitis symptoms. Agents may be used concomitantly or consecutively within the past 30 days.
- For members less than two years of age - Trial of an oral antihistamine, 14 days in duration, that has failed to relieve allergic rhinitis symptoms within the past 30 days.

The DUR Board also voted to allow grandfathering of Singulair® for asthma patients only.

MOTION CARRIED by unanimous approval.

Recommendation 6: Vote to Update Antidepressant PBPA Category and Vote Prior Authorize Pristiq™

The DUR Board recommends further review of this PBPA category and discussion with field specialists.

MOTION TABLED by unanimous approval.

The College of Pharmacy recommends placement of Pristiq into Tier 2 of the currently approved Antidepressant PBPA category. Changes in red on table below.

MOTION CARRIED by unanimous approval.

Dual Acting Antidepressants	
Tier-1	**Tier-2**
bupropion (Wellbutrin®, Wellbutrin SR®, Wellbutrin XL®)	duloxetine (Cymbalta®)
mirtazapine (Remeron®, Remeron SolTab®)	Nefazodone+ (Serzone®)
trazodone (Desyrel®)	venlafaxine (Effexor XR®)
venlafaxine (Effexor®)	desvenlafaxine (Pristiq®)

Blue color indicates current supplemental rebated product.

Idabel Children's Clinic

1307 South Lynn Lane
Idabel, OK 74745
Tel 580-286-**KIDS** (286-5437)
Fax 580-286-3955

Dear Dr. McNeill;

I am writing this letter in response to information I had received about a possible change in the availability of Singulair to my patients on SoonerCare. Since there are no other drugs in this class which may be used as a substitute for Singulair, I wanted to express my concern. I practice in Southeastern Oklahoma and we have high levels of allergens year around. For this reason, many of my patients allergies are managed with multiple medications - most commonly Singulair, with an anti-histamine and a nasal steroid. I would anticipate that if Singulair is no longer available to many of these patients, the rates of sinusitis, ear infections, asthma and pneumonia will significantly increase. Singulair has also been an important therapeutic tool in my treatment of middle ear effusions and has reduced my rate of referral to ENT for tympanostomy tubes. I also believe that Singulair has changed the face of asthma, with marked reductions in hospitalizations and office visits in the asthma patients taking Singulair.

For these reasons, Singulair has been a cornerstone in my treatment of several medical conditions and in the reduction of secondary sequelae, in my patient population. Since there is no substitute for this medication, reduced availability of Singulair will, without a doubt, negatively impact the care of many of my patients. Please consider keeping Singulair available to SoonerCare patients. Thank you for your time.

Sincerely,

Mary Bradley-LeBoeuf, MD, FAAP

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July 3, 2008

Nancy Nesser, PhD
Director of Pharmacy Services
4545 N. Lincoln Blvd., Suite 124
Oklahoma City, Oklahoma 73105

Dear Dr. Nesser:

I am a Medical Director of Laureate Psychiatric Clinic and Hospital in Tulsa. I am a psychiatrist who has been practicing since I left my residency 34 years ago. I have also been involved in research, particularly with depression. I was the Principle Investigator for the Tulsa region for the STAR*D Study - the largest study ever completed with major depression in adults. There were over 4,000 patients in this study. Over 300 of them were treated in Tulsa.

I am writing because it has come to my attention that the State of Oklahoma Medicaid Program is considering adding a second "first fail" tier requirement for generic antidepressants before a brand name antidepressant can be chosen. As will be evident in my comments below, I am opposed to *any* "first fail" requirements, but I am especially opposed to two levels of "first fail" requirements.

I have been on several Pharmacy and Therapeutics Committees for HMO's in my career, and I have often encountered a misconception held by medical professionals who do not treat depressed patients. Because no antidepressant has been found in head-to-head studies to be superior to another antidepressant, these professionals mistakenly assume that these drugs are interchangeable. This is not true. Psychiatrists do not choose antidepressants because one is believed to be more efficacious than another. They make their choices for the following reasons: side effects profiles, prior response to medications, likelihood that the patient will adhere to a medication, and responses by biological relatives to antidepressants. All of these factors are weighed in making a choice for the purpose of maximizing the likelihood that the patient will reach a therapeutic dose, take the medication for an adequate period of time, and attain remission.

Achieving remission (depression symptom severity in the normal range) is now the gold standard for treatment. The earlier a patient can reach remission, the better the long-term outcome. Please see the first attached graph from the STAR*D study. As you can see, remission rates are relatively respectable in the first two trials of an antidepressant. But if the patient fails those two trials, remission rates drop dramatically. Failure to attain remission also has economic consequences, as demonstrated in the second graph. The more times a patient fails an antidepressant trial, the higher the costs for treating those patients.

Physicians need to make their choices based on the patient's past response to medications, side effects (desired or undesired), and genetic histories. Requiring "first fail" trials inhibits the freedom to make these choices, thereby increasing the possibility that the patient will not remit or will not adhere to the first or second trial of medication.

Finally, we must always keep in mind that depression is not a benign illness. As long as they remain depressed they have been found to be heavy utilizers of medical services. Research has also shown that depressed patients are as *physically* impaired as patients with congestive heart failure, their incidence of short-term disability days in the workforce is among the highest for any disease state, and are they are highly vulnerable to cardiovascular and immunological disorders. Finally, 15% eventually commit suicide.

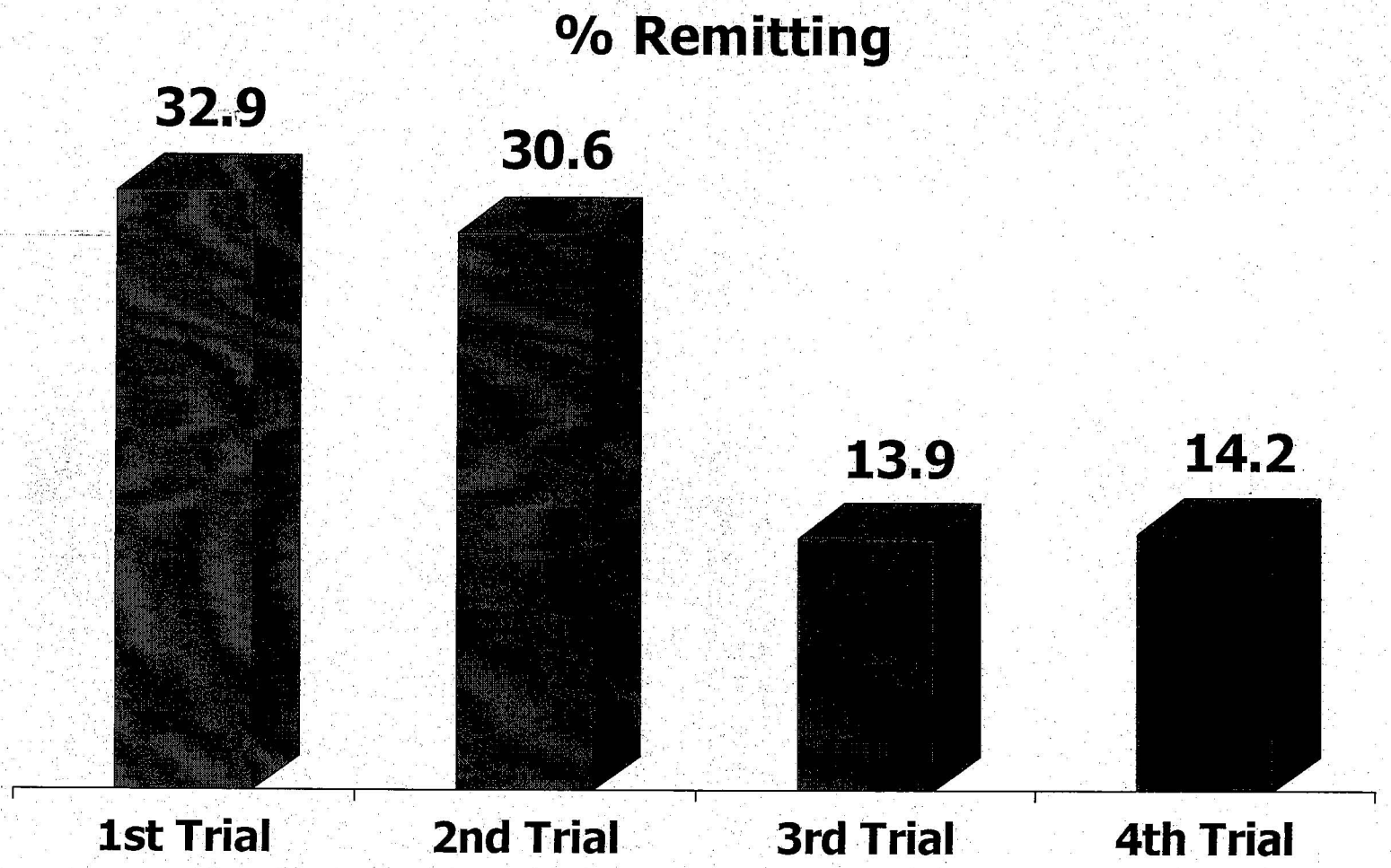
I would be glad to provide more information at requests. Also, I would be pleased to attend any meetings in which you will discuss this issue and answer any questions you may have.

Respectfully,

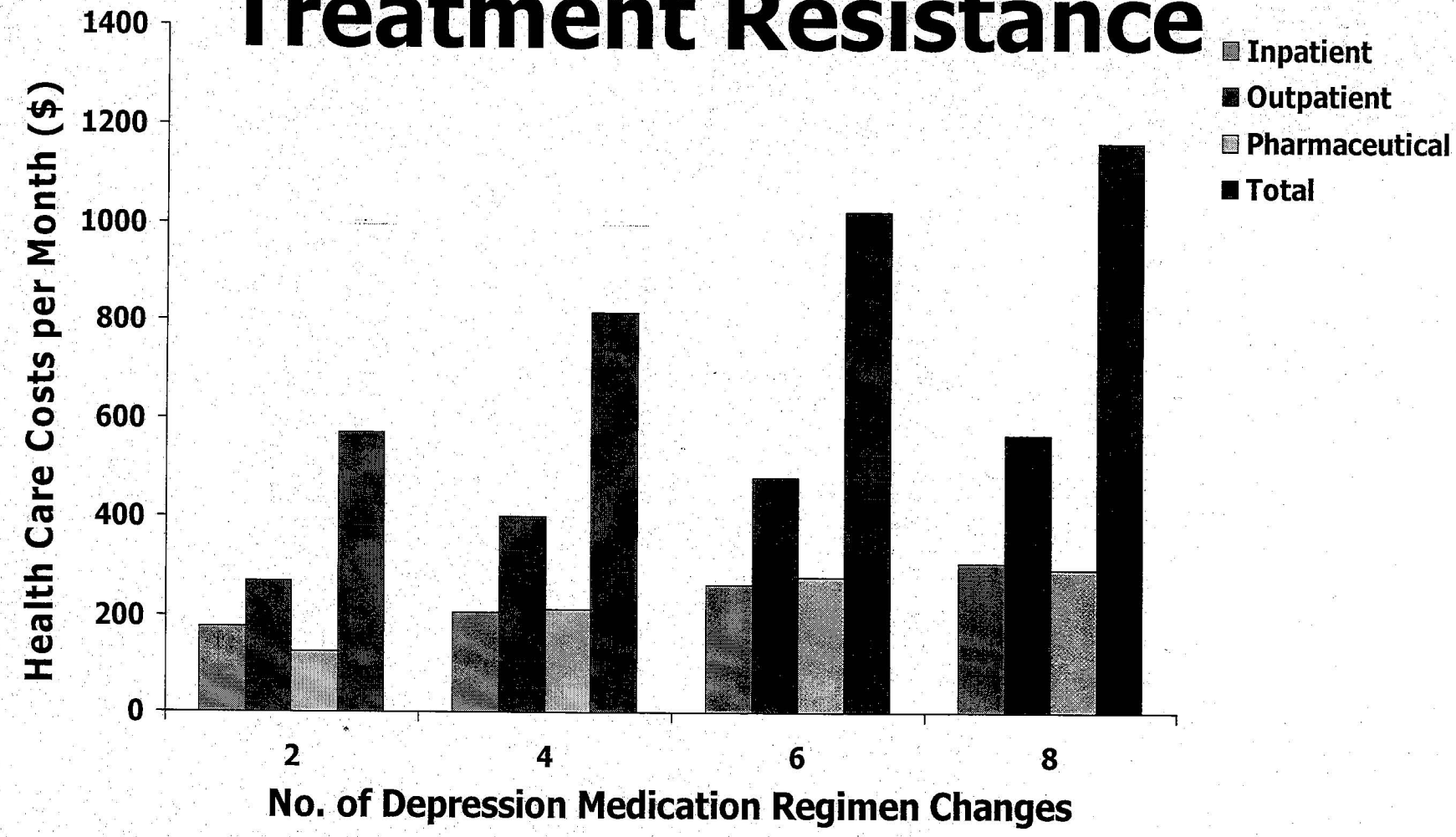
Jeff Mitchell, M.D.
Medical Director

Enclosures

STAR*D Remission Rates for Four Successive Antidepressant Trials

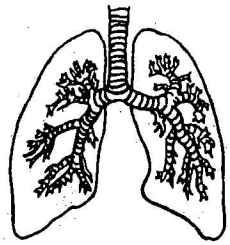


Medical Expenditures Increase With Increasing Degrees of Treatment Resistance



Russell JM, et al. ***J Clin Psychiatry*** **65(3):341-347..**

NORMAN IMES, M.D.
LYNN HEALTH SCIENCE INSTITUTE



DIPLOMAT: AMERICAN BOARD OF INTERNAL MEDICINE
DIPLOMAT: AMERICAN BOARD OF INTERNAL MEDICINE-PULMONARY DISEASES
FELLOW, AMERICAN COLLEGE OF CHEST PHYSICIANS
CONSULTANT IN: DISEASES OF THE CHEST

3555 N.W. 58TH STREET, SUITE 800 • OKLAHOMA CITY, OKLAHOMA 73112

July 10, 2008

John Muchmore, M.D.
3366 NW Expressway, 5th Floor
Oklahoma City, OK 73112

Dear John:

I wanted to make a few comments regarding my visit to the drug utilization review committee on 7-9-08. First of all, I wanted to commend you and the other committee members for your efforts. Drug utilization review is a daunting task which requires not only knowledge of your own field, but also a working knowledge of other areas of medicine. This is a significant time commitment which requires continued efforts to stay abreast of many different developments in medicine.

At the conclusion of the section on Singulair authorization, as I understand the final draft and vote, a patient with asthma must have failure of inhaled corticosteroids and then be placed on long acting beta agonists and fail before they would qualify for authorization of Singulair. If my recollection of the proceedings is not accurate, since I have not seen the final draft, my comments may have no meaning. However, I did give the committee a printout of the GINA guidelines and that recommendation is not consistent with the guidelines. For patients that have mild, persistent asthma, first line therapy is inhaled corticosteroids according to international guidelines NAEPP and GINA and also most other expert reviewers such as the Medical Letter. Singulair is viewed as an alternative drug for a variety of reasons such as improved compliance and a better responsiveness in children, particularly children who may not be adept at using inhalers. There are numerous studies from Merck and others that show asthma control days are basically equivalent between inhaled corticosteroids and montelukast. This includes the New England Journal of Medicine article which was discussed and in my opinion shows bias in the selection process. Patients were chosen to be in the study who had the best response to bronchodilator and also who were already controlled on inhaled corticosteroid therapy. Obviously if a group of patients was studied that was on montelukast as monotherapy with good control and they were removed from montelukast and switched to inhaled corticosteroids, one would, conversely, expect an increased rate of exacerbations.

TELEPHONE (405) 942-6620 • FAX (405) 601-8725

Depending upon the source cited and how the definition of "non-responder" is defined, 20% to at least 40% of patients do not respond to inhaled corticosteroids. Under the scenario which was adopted, patients would then have a long acting beta agonist added for their mild persistent asthma which is not consistent with the international guidelines for asthma management. In addition, Advair is substantially more expensive than Singulair, so the argument that this is cost effective would not seem to be valid (see below). I continue to have serious concerns about the use of long acting beta agonists. There is a long litany of studies in the literature indicating the risk of using long acting beta agonists. As we learn more about the genetic basis for asthma, it appears the "normal" phenotype is particularly susceptible to the adverse effects of long acting beta agonists. Patients who are homozygous for arginine at the 16th position of the beta receptor have a more potent response to inhaled beta agonist, but at the same time develop tachyphylaxis and over a period of time may and frequently do actually get worse with continued use of the drug. Whether this is the cause for increased deaths and increased hospitalization and exacerbations in asthma therapy with these drugs is not known. Obviously this is an important study that needs to be done.

It appears the particular article that provoked the black box warning on these drugs was the SMART trial published in Chest in February of 2006 under the lead author, Nelson. This is a GSK sponsored safety trial to determine the safety of long acting beta agonists. This trial was terminated early with less than half the expected enrollees of 60,000 because of a remarkable increased death rate in the salmeterol group. This included patients who had concomitant therapy with inhaled corticosteroids, as well as patients who had asthma of all severities, including mild asthma. The argument has been made that inhaled corticosteroids may protect from the adverse effects of long acting beta agonists, but that remains to be proven. It also should be considered that since 20% to 40% of patients do not respond to inhaled corticosteroids anyway and we do not know if this sub-group would be protected from risks of beta agonists.

The difficulty with asthma studies is that we are dealing with a heterogenous population with many different genotypes and phenotypes manifested in every patient. The object of therapy is to find the best treatment for that particular patient. Cost considerations are important, but in most cases the best medical treatment is associated with a decrease in long term cost and adverse events.

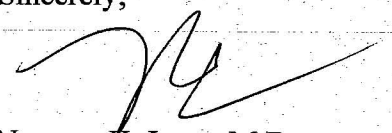
International guidelines in every field of medicine are developed by expert panels who make a genuine effort to review the literature in a unbiased way. We are always on relatively safe ground if we adhere to these guidelines since they do have the power of "community standard". If we deviate from those guidelines in our management of patients, I think we need to have a very good reason for doing so.

Although I understand the use of pharmacists to help develop these drug utilization protocols, there are serious limitations in their abilities. That was obvious when you raised the very appropriate question about how the committee could make a recommendation for a drug which has a black box warning by the FDA such as the long acting beta agonist. Her response was inadequate and not based on any medical literature which you can see is considerable based on the metaanalysis that I provided you from the Salpeter article in the Annals of Internal Medicine, 2006.

The other concern that I have after listening to the drug utilization committee review of Singulair is that there appears to be a lack of full disclosure to the committee. It appears as an outside observer that Singulair has a certain cost to the system each year, but in addition there is a considerable rebate and/or discount for Singulair to the system. The rebate mentioned by the pharmacist seems to be absent from the data, so it appears the committee is being asked to make economic decisions about which drugs to provide based on a drug cost that is not a true reflection of the cost to the system. I find that a bit bothersome.

If my understanding of the final draft is correct, the use of long acting beta agonists as add on therapy for mild persistent asthma is likely to considerably increase the cost to the system, as well as potentially place patients at increased risk of adverse events such as hospitalization and death. It would therefore seem prudent to readdress this issue as soon as possible and develop a protocol which is consistent with international asthma treatment guidelines developed by the NAEPP and GINA.

Sincerely,



Norman K. Imes, M.D.
Medical Director, Lynn Institute
Clinical Professor of Medicine, OU Health Sciences Center
Diplomate American Board of Internal Medicine, Pulmonary Disease
Diplomate American Board of Internal Medicine, Sleep Medicine

NKI/jee
Cc: Thomas Kuhls, M.D.
Dan McNeill, Ph.D., PA-C

Addendum: (Drugstore.com)
Pricing:

Advair 500/50 (one month)	253.99
Advair 250/50 (one month)	196.00
Advair 100/50 (one month)	165.00

Singulair (without discount or rebate)

Singulair 4 mg (one month)	108.01
Singulair 5 mg (one month)	105.99
Singulair 10 mg (one month)	112.25

Building *Lives*

Dr. Dan McNeill, Ph.D., PA-C
Chair of Drug Utilization Review Board
Oklahoma Health Care Authority
4545 North Lincoln Boulevard, Suite 124
Oklahoma City, Oklahoma 73105

13 July 2008

RE: Antidepressant Category Review at 9 July DUR Board Meeting

Dr. McNiell:

Healthcare costs are continuing to rise, and the disparity between those that can access the best care and those who struggle to get the care they need continues to grow. Managing costs is no longer a choice, but a necessity, and as advocates for both quality and access to care we understand the difficulties and the disagreements that surround this discussion. While we will continue to dialogue with the Drug Utilization Review board and the Oklahoma Health Care Authority about access to mental health care and medicines we write you today to discuss the response of the board to a speaker at the July 9th DUR board meeting.

The DUR board meeting left us deeply troubled by the response of board members to the testimony of a Medicaid client and self-proclaimed mental health consumer. The story which Susie Seymour was kind enough to share with the board that evening was discounted and her commentary was rudely brushed aside by board members as irrelevant to the discussion at hand.

Such comments and behavior by board members suggests that there is a lack of understanding of their role and purpose within the broader picture. Ms. Seymour's story was powerful and important because it reminded us of why we were discussing and debating the anti-depressant prior authorization proposal. She bravely told of her struggles and difficulties stabilizing on her medications and gave a voice to the Medicaid clients who rely on this important program every day. The callous disregard that the board members communicated was troubling because her story reminds us of how difficult finding the right medication can be, and that adding additional impediments to choices that physicians and their patients make is an imprudent step.

1870 South Boulder, Tulsa, Oklahoma 74119
Telephone (918) 585-1213 • Fax (918) 585-1263
www.mhat.org

MENTAL HEALTH ASSOCIATION IN TULSA

United Way

As advocates for Oklahoman's with mental illness we must constantly struggle against the stigma of mental illness. But it is disturbing that we must fight physicians and pharmacists to treat people with mental illness with the respect that they deserve as fellow people.

We request a formal apology to Ms. Seymour from the DUR board. In addition to the deserved apology we ask that the board make the commitment to Ms. Seymour, along with the other people who rely upon Medicaid, that they will always maintain the person as their top priority, not the dollar, or worse, the supplemental rebate.

Your consideration and further action is appreciated.

Sincerely,

Michael W. Brose, MSW
Executive Director

Paul G. Davis
Director of Advocacy

cc: Susie Seymour
Mike Fogarty
Dr. Nancy Nesser
Debbie Spaeth
Kaye Rote
Karina Forrest

MIKE FOGARTY
CHIEF EXECUTIVE OFFICER

BRAD HENRY
GOVERNOR

STATE OF OKLAHOMA
OKLAHOMA HEALTH CARE AUTHORITY

July 29, 2008

Mr. Michael W. Brose, MSW
Executive Director
And
Mr. Paul G. Davis
Director of Advocacy
Mental Health Association in Tulsa
1870 South Boulder
Tulsa, OK 74119

Dear Mr. Brose and Mr. Davis:

Thank you for your letter of July 13, 2008 citing your concern regarding the reception Ms. Susie Seymour received following her testimony at the July 9, 2008 meeting of the Drug Utilization Review (DUR) Board. As Chair of the DUR Board, I applaud Ms. Seymour for her willingness to testify and for her advocacy on behalf of those with mental illness.

I was troubled that my recollection of Ms. Seymour's testimony and comments from DUR Board members differed significantly from what you described in your letter. After listening to the audio tape of the meeting, I am even more troubled that you could make such comments given that Board members agreed with the point of Ms. Seymour's presentation. Specifically, Board members agreed that a patient stable on a drug from a higher tier would not have to return to a lower tiered medication. Also explicitly evident on the audio tape is compassion expressed by DUR Board members towards: 1) respecting Ms. Seymour's desire not to switch to medications previously determined to be ineffective, 2) stating that her point was taken and 3) her having to endure six years of medication trials before finding the right "cocktail".

As indicated during the DUR meeting, we would be reaching out to experts in the field of mental health before making any decisions. I willingly make the commitment to you that consultation will include members of the Department of Psychiatry, University of Oklahoma College of Medicine, Dr. Brent Bell of the DUR Board and the Oklahoma State Department of Mental Health and Substance Abuse.

Finally, if Ms. Seymour still feels DUR Board members were not supportive of her plight, I would welcome the opportunity to speak with her directly. However, after hearing her testimony and the Board's response in person and on audio tape, I do not feel a formal apology is needed in that it was clear Board members indeed understood and were empathetic to Ms. Seymour's needs.

Sincerely,

Daniel L. McNeill, Ph.D., P.A.-C
Chair
Drug Utilization Review Board

cc: Mr. Mike Fogarty
Dr. Nancy Nesser
DUR Board

Appendix B

Retrospective Drug Utilization Review Report

Claims Reviewed for April 2008

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Total # of messages returned by system when no limits were applied	41,186	59,520	1,065,531	32,233
Limits which were applied	Established, Major, Males and Females, Age 22-35	Males and Females, 22-40 years of age, Antidepressants-SSRIs	Contraindicated, Hepatic Disease, Males and Females 36-45 years old	High Dose only, 3120 Digitalis, Males and Females 0-150
Total # of messages after limits were applied	39	118	97	4
Total # of members reviewed after limits were applied	39	108	83	4

LETTERS			
Prescribers		**Pharmacies**	
Sent	**Responded**	**Sent**	**Responded**
64		11	

Retrospective Drug Utilization Review Report

Claims Reviewed for January 2008

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Limits which were applied	Established, Major, Males and Females, Age 19-37	Narcotics, Males and Females, Age 22-24	Contraindicated, Asthma, Males and Females, Age 36-42	High Dose, Abilify and Geodon, Males and Females, Age 44-150

Response Summary (Prescriber)
Letters Sent: 112
Response Forms Returned: 79

The response forms returned yielded the following results:

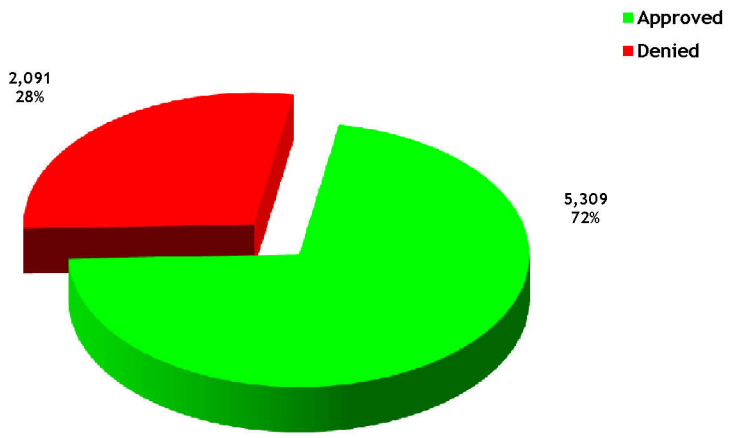
17 (22%)	*Record Error—Not my patient.*
11 (14%)	*No longer my patient.*
2 (3%)	*Medication has been changed prior to date of review letter.*
23 (29%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
12 (15%)	*I am aware of this situation and will plan to continue monitoring therapy.*
14 (18%)	*Other*

Response Summary (Pharmacy)
Letters Sent: 36
Response Forms Returned: 23

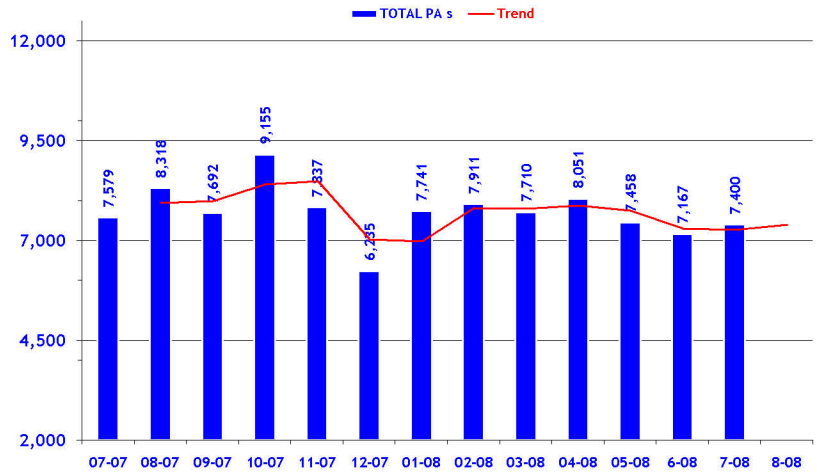
The response forms returned yielded the following results:

1 (4%)	*Record Error—Not my patient.*
4 (17%)	*No longer my patient.*
2 (9%)	*Medication has been changed prior to date of review letter.*
1 (4%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
10 (43%)	*I am aware of this situation and will plan to continue monitoring therapy.*
5 (22%)	*Other*

PRIOR AUTHORIZATION ACTIVITY REPORT
July 2008



PRIOR AUTHORIZATION REPORT
July 2007 – July 2008



Activity Audit for

July 01, 2008 Through July 31, 2008

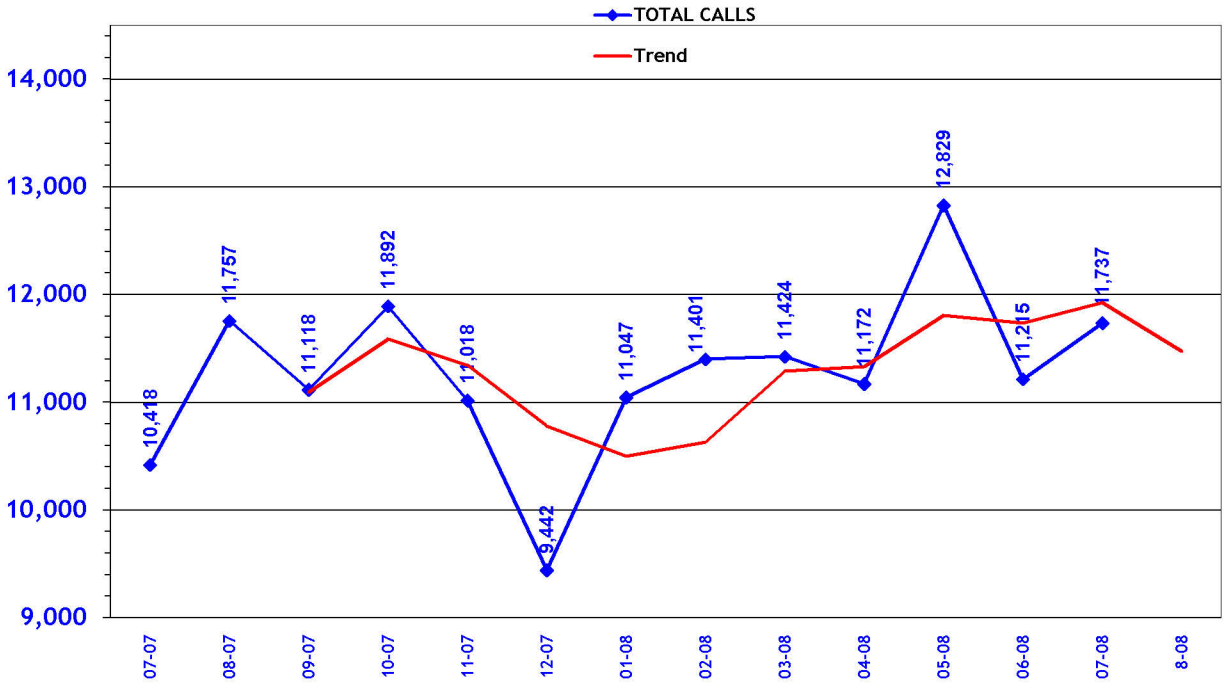
	Average Length of Approvals in Days	Approved	Denied	Total
ACE Inhibitors	23	7	3	10
Angiotensin Receptor Antagonist	348	24	89	113
Antidepressant	282	168	232	400
Antihistamine	90	250	175	425
Antiulcers	8	18	2	20
Anxiolytic	94	3,212	400	3,612
Calcium Channel Blockers	12	3	2	5
Growth Hormones	176	29	1	30
HTN Combos	183	6	7	13
Insomnia	93	25	17	42
Nsaids	212	22	41	63
Plavix	355	113	23	136
Stimulant	207	476	196	672
Others	84	956	903	1,859
Emergency PAs		0	0	0
Total		**5,309**	**2,091**	**7,400**
Overrides				
Brand	302	12	8	20
Dosage Change	7	331	29	360
High Dose	104	3	0	3
Ingredient Duplication	8	1	1	2
Lost/Broken Rx	6	78	4	82
Nursing Home Issue	10	47	2	49
Other	56	14	3	17
Quantity vs. Days Supply	120	14	2	16
Stolen	15	7	0	7
Overrides Total		**506**	**48**	**554**

Denial Reasons

Lack required information to process request.	1,764
Unable to verify required trials.	990
Not an FDA approved indication/diagnosis.	157
Does not meet established criteria.	140
Considered duplicate therapy. Member has a prior authorization for similar medication.	104
Requested dose exceeds maximum recommended FDA dose.	97
Member has active PA for requested medication.	40
Drug Not Deemed Medically Necessary	6
Medication not covered as pharmacy benefit.	5
Duplicate Requests	467
Changes to existing*	606

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

CALL VOLUME MONTHLY REPORT
July 2007 – July 2008



Appendix C

Vote to Prior Authorize Voltaren® Gel (diclofenac sodium)

Oklahoma Health Care Authority
August 2008

Manufacturer	Novartis
FDA Classification	NSAID
Status	Prescription Only

Summary

Voltaren® gel is a topical analgesic gel containing 1% diclofenac sodium indicated for the relief of joint pain associated with osteoarthritis amenable to topical treatment, such as of the knees and of the hands. It has not been evaluated for use in the spine, hip or shoulder.

Dosage for the lower extremities is 4g to affected area 4 times daily (no more than 16g to a single joint daily), and for upper extremities is 2g to affected area 4 times daily (no more than 8g to a single joint daily). Total dose should not exceed 32g per day, over all affected areas.

Recommendations

The College of Pharmacy recommends prior authorization of Voltaren® Gel and placement in the Tier 2 NSAID product. Approval will be based on clinical documentation of inability to take Tier 1 products and supporting information regarding the medical necessity of a topical formulation.

Appendix D

30 Day Notice to Prior Authorize ESAs

Oklahoma Health Care Authority

August 2008

FDA Indications

Epogen® and Procrit® (epoetin alfa)

1. Treatment of Anemia of Chronic Renal Failure Patients
2. Treatment of Anemia in Zidovudine-treated HIV-infected Patients
3. Treatment of Anemia in Cancer Patients on Chemotherapy
4. Reduction of Allogeneic Blood Transfusion in Surgery Patients

Aranesp® (darbepoetin alfa)

1. Treatment of anemia associated with chronic renal failure (patients on dialysis or patients not on dialysis)
2. Treatment of anemia in patients with non-myeloid malignancies where anemia is due to the effect of concomitantly administered chemotherapy.

Off Label Uses:

- Anemia - Congestive heart failure
- Anemia - Critical illness
- Anemia - Rheumatoid arthritis
- Anemia - Multiple myeloma
- Anemia - Myelodysplastic syndrome
- Anemia due to radiation
- Anemia during the puerperium
- Anemia of chronic disease - Neoplastic disease
- Anemia of prematurity
- Anemia - Hepatitis C, In patients being treated with a combination of ribavirin and interferon alfa or ribavirin and peginterferon alfa
- beta Thalassemia
- Blood unit collection for autotransfusion

Center for Medicare and Medicaid Services (CMS) Guidelines for Medicare Part B[1]

Chronic Kidney Disease (CKD) related Anemia

EPO and Aranesp are covered under the Part B benefit for the treatment of symptomatic anemia in patients with ESRD who are on dialysis. Generally, patients should have a hematocrit less than 30% or hemoglobin less than 10 g/dL. Patients with ESRD who have been receiving EPO/Aranesp therapy should have a hematocrit between 30% and 36%.

Non CKD-related Anemia

CMS has determined that there is sufficient evidence to conclude that erythropoiesis stimulating agent (ESA) treatment is not reasonable and necessary for beneficiaries with certain clinical conditions, either because of a deleterious effect of the ESA on their underlying disease or because the underlying disease increases their risk of adverse effects associated with ESA use. These conditions include:

1. Any anemia in cancer or cancer treatment patients due to folate deficiency, B-12 deficiency, iron deficiency, hemolysis, bleeding, or bone marrow fibrosis;
2. The anemia associated with the treatment of acute and chronic myelogenous leukemias (CML, AML), or erythroid cancers;
3. The anemia of cancer not related to cancer treatment;
4. Any anemia associated only with radiotherapy;
5. Prophylactic use to prevent chemotherapy-induced anemia;
6. Prophylactic use to reduce tumor hypoxia;
7. Patients with erythropoietin-type resistance due to neutralizing antibodies; and
8. Anemia due to cancer treatment if patients have uncontrolled hypertension.

Anemia due to Myelosuppressive Anticancer Chemotherapy

CMS has determined that ESA treatment for the anemia secondary to myelosuppressive anticancer chemotherapy in solid tumors, multiple myeloma, lymphoma and lymphocytic leukemia is only reasonable and necessary under the following specified conditions:

1. The hemoglobin level immediately prior to initiation or maintenance of ESA treatment is < 10 g/dL (or the hematocrit is < 30%).
2. The starting dose for ESA treatment is the recommended FDA label starting dose, no more than 150 U/kg/three times weekly for epoetin and 2.25 mcg/kg/weekly for darbepoetin alpha. Equivalent doses may be given over other approved time periods.
3. Maintenance of ESA therapy is the starting dose if the hemoglobin level remains below 10 g/dL (or hematocrit is < 30%) 4 weeks after initiation of therapy and the rise in hemoglobin is > 1g/dL (hematocrit > 3%).
4. For patients whose hemoglobin rises <1 g/dl (hematocrit rise <3%) compared to pretreatment baseline over 4 weeks of treatment and whose hemoglobin level remains <10 g/dL after the 4 weeks of treatment (or the hematocrit is <30%), the recommended FDA label starting dose may be increased once by 25%. Continued use of the drug is not reasonable and necessary if the hemoglobin rises <1 g/dl (hematocrit rise <3 %) compared to pretreatment baseline by 8 weeks of treatment.
5. Continued administration of the drug is not reasonable and necessary if there is a rapid rise in hemoglobin > 1 g/dl (hematocrit > 3%) over 2 weeks of treatment unless the hemoglobin remains below or

subsequently falls to < 10 g/dL (or the hematocrit is < 30%). Continuation and reinstitution of ESA therapy must include a dose reduction of 25% from the previously administered dose.

6. ESA treatment duration for each course of chemotherapy includes the 8 weeks following the final dose of myelosuppressive chemotherapy in a chemotherapy regimen.

Other National Guidelines for ESA's[2,3]

- **National Kidney Foundation's** 2007 KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Anemia in Chronic Kidney Disease, updated 2007:
  - Defines anemia as: <13.5 g/dL in adult males and <12.0 g/dL in adult females.
  - In patients with CKD target range for hemoglobin (Hb) should be in the range of 11.0 to 12.0 g/dl.
  - Target Hb should not exceed 13.0 g/dL in ESA-treated patients.
- Clinical Practice Guidelines of the **American Society of Clinical Oncology** and the **American Society of Hematology**, updated Aug 2007:
  - Epoetin is recommended for patients with chemotherapy-associated anemia whose Hb is <10 g/dl at a starting dose of 150U/kg three times a week for 4 weeks. Dosing weekly with 40,000U is also acceptable.
  - Darbepoetin is recommended for patients with chemotherapy-associated anemia whose Hb is <10 g/dl at a starting dose of 2.25µg/kg weekly or 500µg every 3 weeks.
  - Target Hb range should not exceed 12 g/dl.
  - For patients whose Hb level fails to respond to adequate doses after 6-8 weeks, continued treatment with epoetin does not appear to be of benefit.
  - Recommend against the use of ESAs to treat anemia associated with malignancy, or the anemia of cancer, among patients with solid or non-myeloid malignancies who are not receiving concurrent chemotherapy.

Recent Developments with Erythropoiesis-Stimulating Agents[4, 5]

On November 8, 2007, the FDA approved new labeling strengthening the boxed warning and warning sections of labeling for epoetin and darbepoetin. This updated labeling is shown at the end of this section.

On November 30, 2007, the FDA was notified by the manufacturer of findings from the Preoperative Epirubicin Paclitaxel Aranesp Study (PREPARE). The PREPARE study enrolled patients with primary breast cancer that were to undergo chemotherapy prior to surgery. These patients were randomly assigned to receive Aranesp or no Aranesp.

On December 4, 2007, the FDA was notified by the manufacturer of findings from the GOG-191 study. This study enrolled patients with cervical cancer treated with chemotherapy and radiation and were assigned to receive ESA or transfusions. The study stopped enrolling patients because of a higher rate of potentially life-threatening blood clots in the patients receiving an ESA.

Both the PREPARE study and the GOG-191 study showed higher rates of death and/or tumor progression in patients receiving ESA compared to those who did not receive ESA therapy.

On March 13, 2008, the FDA's Oncologic Drugs Advisory Committee (ODAC) recommended continuing the indication of treatment of chemotherapy-induced anemia in cancer patients, but recommended changes to the safety labels that would restrict use for cancer patients.

On July 31, 2008 the FDA instructed the manufacturers to make the following changes to the labels for erythropoisis-stimulating factor products:

- The drugs are "not indicated for those receiving myelosuppressive therapy when the anticipated outcome is cure."
- Therapy should not be initiated at hemoglobin levels of 10 g/dL and above.
- Doses should be withheld if hemoglobin levels exceed a level needed to avoid transfusion.

Black Box Warning applicable for all epoetin and darbepoetin alfa products (11/8/2007)[6]:

WARNINGS: INCREASED MORTALITY, SERIOUS CARDIOVASCULAR and THROMBOEMBOLIC EVENTS, and TUMOR PROGRESSION

Renal failure: **Patients experienced greater risks for death and serious cardiovascular events when administered erythropoiesis-stimulating agents (ESAs) to target higher versus lower hemoglobin levels (13.5 vs. 11.3 g/dL; 14 vs. 10 g/dL) in two clinical studies. Individualize dosing to achieve and maintain hemoglobin levels within the range of 10 to 12 g/dL.**

Cancer:

- **ESAs shortened overall survival and/or time-to-tumor progression in clinical studies in patients with breast, non-small cell lung, head and neck, lymphoid, and cervical cancers when dosed to target a hemoglobin of ≥ 12 g/dL.**
- **The risks of shortened survival and tumor progression have not been excluded when ESAs are dosed to target a hemoglobin of < 12 g/dL.**
- **To minimize these risks, as well as the risk of serious cardio- and thrombovascular events, use the lowest dose needed to avoid red blood cell transfusions.**
- **Use only for treatment of anemia due to concomitant myelosuppressive chemotherapy.**
- **Discontinue following the completion of a chemotherapy course.**

Perisurgery: **PROCRIT® increased the rate of deep venous thromboses in patients not receiving prophylactic anticoagulation. Consider deep venous thrombosis prophylaxis.**

Utilization January 1, 2007 thru June 30, 2007

January 2007 through June 2007

BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	COST
Aranesp **(darbepoetin)**	34	54	9,44	14	$114,485.07
Epogen **(epoetin)**	42	260	1,186	21	$ 50,530.10
Procrit **(epoetin)**	183	901	4,690	66	$189,343.02
Totals	259	1,214	6,820	100*	$354,358.19

*Unduplicated members

January 2008 through June 2008

BRAND NAME	CLAIMS	UNITS	DAYS	MEMBERS	COST
Aranesp **(darbepoetin)**	31	68	680	8	$143,140.58
Epogen **(epoetin)**	27	145	833	10	$ 45,991.40
Procrit **(epoetin)**	181	787	4,372	70	$158,635.39
Totals	239	1,000	5,885	87*	$347,767.37

*Unduplicated members

For pharmacy point-of-sale claims for the first half of 2008, 26% of the members did not appear to have an FDA approved diagnosis on record. The majority of potentially related diagnoses were for unspecified anemias or anemias related to other chronic diseases.

Outpatient 1500 & UB04 Claims - January 2007 through June 2007

HCPCS Code	CLAIMS	MEMBERS	UNITS	UNIT DESCRIPTION
J0881	**528**	**182**	**152,621**	**1 unit = 1 mcg**
J0882	**11**	**7**	**2,680**	**1 unit = 1 mcg**
J0885	**339**	**50**	**9,119**	**1 unit = 1000 units**
J0886	**125**	**19**	**4,817**	**1 unit = 1000 units**
Totals	**1,003**	**258**		

J0881 – Injection, darbepoetin alfa – non-ESRD
J0882 – Injection, darbepoetin alfa – ESRD
J0885 – Injection, epoetin alfa – non-ESRD
J0886 – Injection, epoetin alfa – ESRD

Outpatient 1500 & UB04 Claims - January 2008 through June 2008

HCPCS Code	CLAIMS	MEMBERS	UNITS	UNIT DESCRIPTION
J0881	**217**	**90**	**59,937**	**1 unit = 1 mcg**
J0882	**17**	**7**	**4,250**	**1 unit = 1 mcg**
J0885	**135**	**27**	**10,213**	**1 unit = 1000 units**
J0886	**22**	**2**	**1,281**	**1 unit = 1000 units**
Totals	**391**	**126**		

Recommendations

The College of Pharmacy recommends the following options for consideration by the DUR Board:

Option 1

Continue to monitor category for the next six months and review.

Option 2

Prior Authorization of these products for all indications:

1. FDA approved indication for specific products.
    a. Treatment of Anemia of Chronic Renal Failure Patients
    b. Treatment of Anemia in Zidovudine-treated HIV-infected Patients
    c. Treatment of Anemia in Cancer Patients on Chemotherapy
        i. Myelosuppressive Chemotherapy-Induced Anemia (Hb 8-10 g/dL) Non-Curative
    d. Reduction of Allogeneic Blood Transfusion in Surgery Patients
2. Most recent Hb levels (and date obtained) should be included on petition. Each approval will be for 8 weeks in duration. Authorization can be granted for up to 8 weeks following the final dose of myelosuppressive chemotherapy in a chemotherapy regimen. Authorization for surgery patients will be for a maximum of 4 weeks.
3. Continuation Criteria:
    a. Continue dose if Hb is ≤ 12.0 g/dL.
    b. If Hb is increasing and approaching 12 g/dL then reduce dose by at least 25%.
    c. If more than 1 g/dL increase (but Hb not greater than upper limits listed below) has occurred in a 2 week period reduce dose by 25 to 50 %.
4. Discontinuation Criteria:
    a. ESRD – Discontinue treatment if Hb is at or above 13.0 g/dL.
    b. All others – Discontinue treatment if Hb is at or above 12 g/dL.
    c. If a minimum increase of 1 g/dL has not been achieved after initial 8 weeks of therapy.
5. Reinitiation Criteria:
    a. If Hb decreases to ≤ 10 g/dL then therapy may be reinitiated at 25 to 50% of the prior dose.

Option 3

Prior authorization of these products for treatment of chemotherapy-induced anemia and all other non-FDA approved indications.

1. Allow claims for both medical and pharmacy to pay if diagnosis is detected in claims history indicating ESRD or HIV. (Perisurgery would require prior authorization due to lack of specific diagnosis coding.)
2. Initiation, Continuation, and Discontinuation Criteria as indicated above would apply for chemotherapy-induced anemia patients.

References

1. CMS Manual System. Pub 100-04 Medicare Claims Processing. Transmittal 1307. July 20, 2007
2. National Kidney Foundation, Inc. <http:/www.kidney.org>.
3. Rizzo Jd, Somerfield MR, Hagerty KL, et al: American Society of Clinical Oncology/American Society of Hematology 2007 Clinical Practice Guideline Update on the Use of Epoetin and Darbepoetin. J Clin Oncol 2007; JCO Early Release 10.1200/JCO.2007.14.3396 on October 22 2007.
4. Food and Drug Administration. Center for Drug Evaluation and Research. Communication about an Ongoing Safety Review. 3 January 2007. 17 July 2008 < http://www.fda.gov/cder/drug/early_comm/ESA.htm>.
5. American Society of Hematology. ODAC Recommends ESAs Continue to be Indicated for Treatment of Chemotherapy-Induced Anemia but with New Restrictions. 14 May 2008. 17 July 2008 <http://www.hematology.org/policy/news/03142008.cfm>.
6. Procrit™ package insert. Website available at: http://procrit.com/impor_safe.html.

Appendix E

30 Day Notice to Prior Authorize Patanase®

Oklahoma HealthCare Authority, August 2008

Manufacturer	Alcon Laboratories, Inc.
Classification	H_1 receptor antagonist nasal spray
Status	Prescription only

Summary

Patanase 0.6% (665mcg of olopatadine hydrochloride in each 100-microliter spray) is an antihistamine nasal spray with selective H_1 receptor antagonist activity. It is specifically indicated for symptom relief of seasonal allergic rhinitis in patients 12 years of age and older for symptomatic relief of seasonal allergic rhinitis. It is available in a 30.5g bottle that contains 240 actuations. The recommended dose is two sprays per nostril twice a day.

Nasal Allergy Products		
Tier 1	***Tier 2***	***Tier 3***
Corticosteroids		
Fluticasone (Flonase®)		**budesonide (Rhinocort® AQ)**
Flunisolide (Nasalide®, Nasarel™)		
beclomethasone (Beconase® AQ)		
ciclesonide (Omnaris™)		
mometasone (Nasonex®)		
fluticasone (Veramyst™)		
triamcinolone (Nasacort® AQ)		
Other		
ipratropium bromide (Atrovent®)		
olopatadine (Patanase®)		
azelastine (Astelin®)		

Moved to Tier 1 due to supplemental rebates.

Recommendations

The College of Pharmacy recommends prior authorization of Pantanase® and placement as a Tier 3 nasal allergy product. Approval will be based on the following criteria:

1. The following criteria are required for approval of a Tier 2 product (or a Tier 3 product if no Tier 2 exists):
    a. Documented adverse effect or contraindication to the preferred products.
    b. Failure with at least two Tier 1 medications defined as no beneficial response after at least two weeks each of use during which time the drug has been titrated to the recommended dose (all available Tier 1 corticosteroids should be tried prior to approval of higher Tiered products).
2. The following criteria are required for approval of a Tier 3 product:
    a. All Tier 2 criteria must be met.
    b. Failure with all available Tier 2 products defined as no beneficial response after at least two weeks each of use during which time the drug has been titrated to the recommended dose.
3. Approvals will be for the duration of three months, except for members with chronic diseases such as asthma or COPD, in which case authorizations will be for the duration of one year.

Appendix F

Annual Review of Anti-Ulcers and 30 Day Notice to Prior Authorize Protonix Suspension®

Oklahoma Health Care Authority
August 2008

Current Prior Authorization of Anti-Ulcers

Anti-Ulcer Medications	
The following products requires prior authorization with a special reason for use: ▪ ranitidine (Zantac) – effervescent tablets and capsules ▪ brand omeprazole 40mg (Prilosec 40mg caps)	
Tier 1	**Tier 2**
omeprazole (10 and 20 mg caps)	esomeprazole (Nexium Caps and I.V.)*
omeprazole/antacid (Zegerid Caps)	omeprazole/antacid (Zegerid Packets)*
lansoprazole (Prevacid) capsules	lansoprazole (Prevacid ODT and Granules)*
	pantoprazole sodium (Protonix Tabs and I.V.)*
	rabeprazole sodium (Aciphex Tabs)

Blue color indicates Supplemental Rebate Participation * Non-tablet dosage forms require reason for use.

Approval Criteria

- Documented recent trial of a Tier 1 medication with inadequate results or adverse effect, or
- Documented contraindication to the Tier 1 medications, or
- Documented FDA-approved indication for which Tier 1 products are not indicated

Quantity Limits

- Omeprazole 10 mg: #60 for 30 days
- Omeprazole 20 mg: #120 for 30 days
- All other PPI's: #30 for 30 days

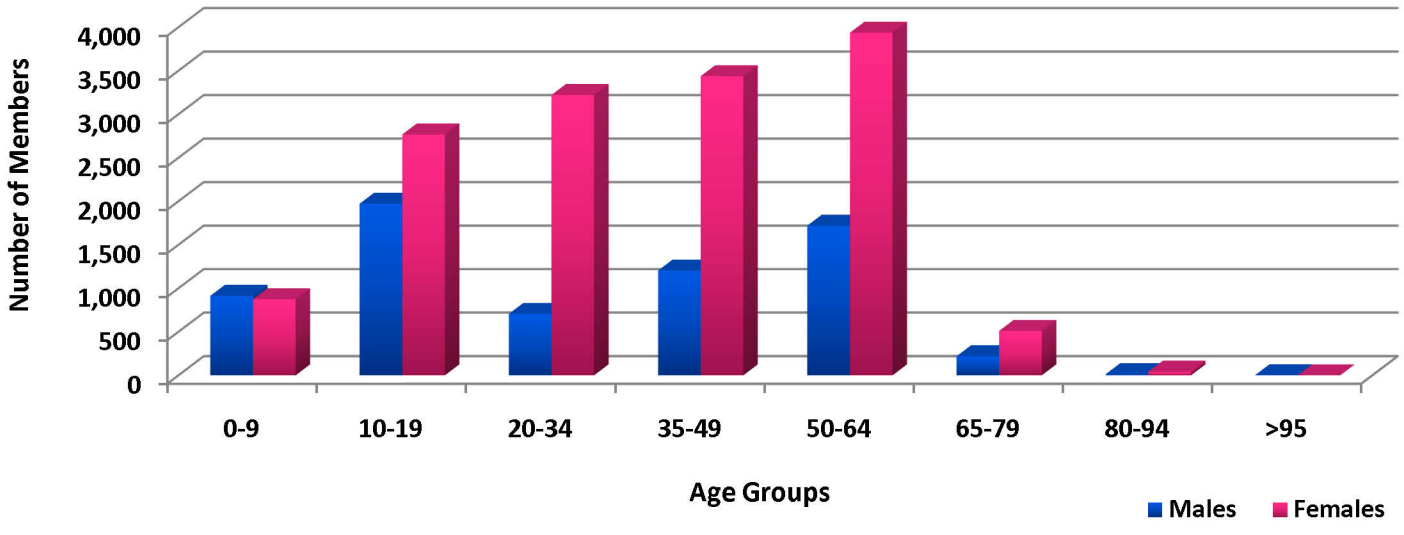
Trends in Utilization of Anti-Ulcer Medications

Fiscal Year	Members	Claims	Cost	Cost/Claim	Perdiem	Units	Days
2007	21,391	92,488	$8,967,028.30	$96.95	$3.10	3,263,177	2,887,962
2008	22,014	94,571	$9,803,753.47	$103.67	$3.17	3,554,418	3,090,095
Change	623	2,083	$836,725.17	$6.72	$0.07	291,241	202,133
Percent Change	2.9 %	2.3 %	9.3 %	6.9 %	2.3 %	8.9 %	7.0 %

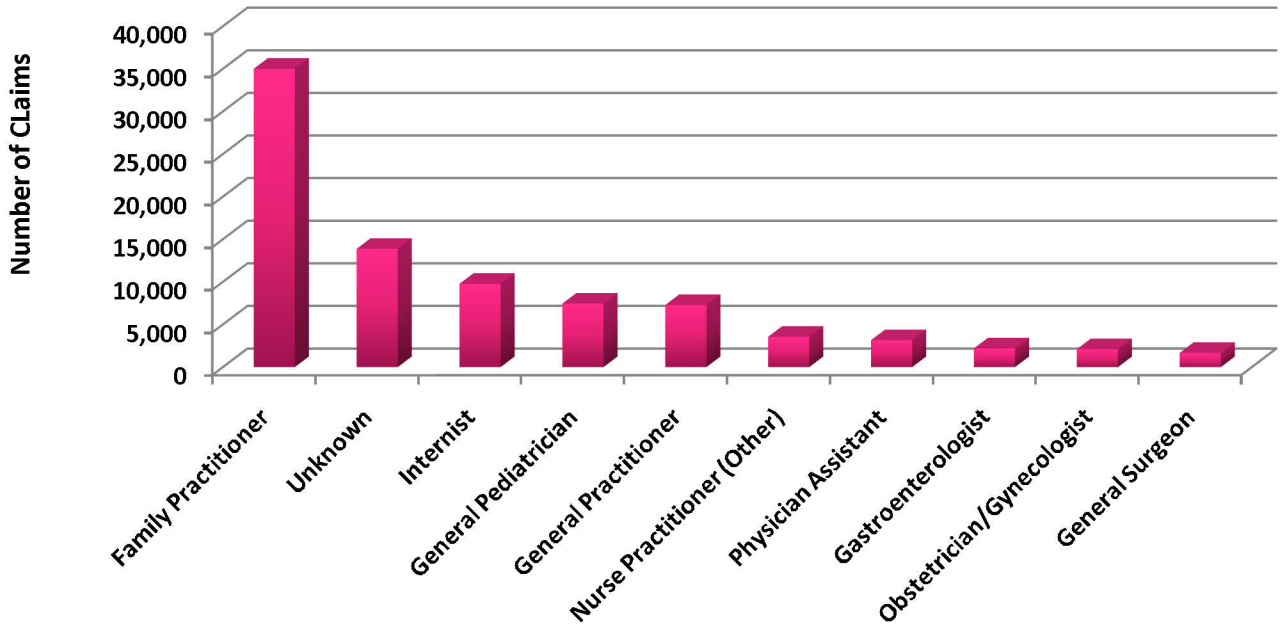
Utilization Anti-ulcer Medications during Fiscal Year 2008

Medication	Claims	Members	Units	Days	Cost	Units/ Day	Claims/ Member	Perdiem
OMEPRAZOLE CAP 20MG	35,916	10,247	1,654,763	1,232,963	$910,627.62	1.34	3.51	$0.74
PREVACID CAP 30MG DR	25,019	6,618	810,353	787,437	$4,084,966.92	1.03	3.78	$5.19
NEXIUM CAP 40MG	9,605	1,637	316,819	308,819	$1,596,423.84	1.03	5.87	$5.17
PROTONIX TAB 40MG	8,451	3,035	279,088	277,128	$1,118,008.50	1.01	2.78	$4.03
PREVACID CAP 15MG DR	5,327	1,780	160,502	158,962	$818,593.87	1.01	2.99	$5.15
PANTOPRAZOLE TAB 40MG	4,346	1,500	142,643	139,770	$454,301.07	1.02	2.9	$3.25
ACIPHEX TAB 20MG	2,916	496	93,870	92,428	$474,369.10	1.02	5.88	$5.13
PREVACID TAB 15MG STB	985	376	29,409	30,537	$118,770.31	0.96	2.62	$3.89
NEXIUM CAP 20MG	592	137	18,995	18,850	$95,889.53	1.01	4.32	$5.09
OMEPRAZOLE CAP 10MG	470	155	15,334	14,308	$15,891.38	1.07	3.03	$1.11
PROTONIX TAB 20MG	279	117	9,244	9,094	$36,507.35	1.02	2.38	$4.01
PREVACID TAB 30MG STB	161	55	5,318	4,933	$21,637.67	1.08	2.93	$4.39
PRILOSEC OTC TAB 20MG	150	61	6,279	4,602	$4,368.04	1.36	2.46	$0.95
PREVACID GRA 15MG	120	61	3,295	3,555	$16,852.40	0.93	1.97	$4.74
PREVACID 30MG STB	68	28	2,435	2,225	$10,613.41	1.09	2.43	$4.77
PANTOPRAZOLE TAB 20MG	53	25	1,678	1,648	$5,391.12	1.02	2.12	$3.27
PRILOSEC CAP 40MG CR	49	19	2,673	1,398	$9,911.61	1.91	2.58	$7.09
PREVACID GRA 30MG	23	7	900	675	$4,672.80	1.33	3.29	$6.92
NEXIUM GRA 40MG DR	17	6	596	538	$3,095.06	1.11	2.83	$5.75
NEXIUM I.V. SOL 40MG	14	2	62	62	$1,655.23	1	7	$26.70
PROTONIX INJ 40MG	6	4	43	43	$590.50	1	1.5	$13.73
NEXIUM GRA 20MG DR	4	1	120	120	$616.14	1	4	$5.13
TOTALS	94,571	22,014	3,554,419	3,090,095	$9,803,753.47	1.15	4.3	$3.17

Demographics of Members Utilizing Anti-ulcer Medications during Fiscal Year 2008

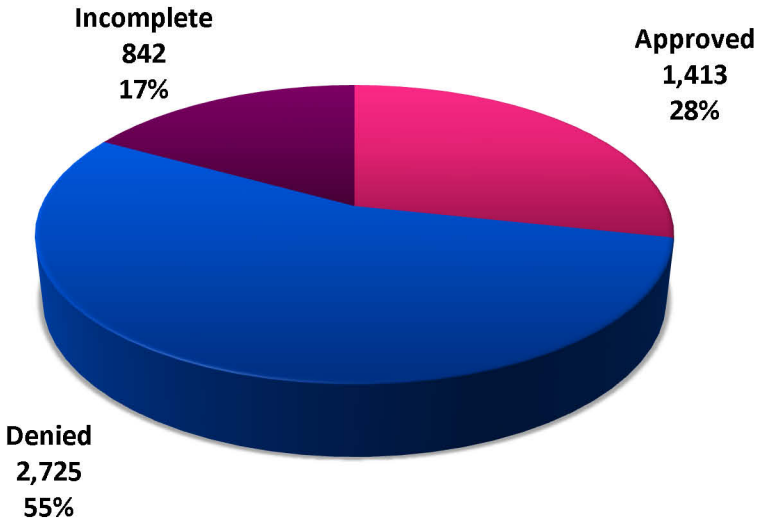


Prescribers of Anti-ulcer Medications during Fiscal Year 2008



Prior Authorization of Anti-ulcer Medications during Fiscal Year 2008

There were a total of 4,980 petitions submitted for this PBPA category during fiscal year 2008. The following chart includes step therapy petitions as well as Refill Too Soon and Quantity Limit Override petitions. Most prior authorizations for this category are processed through Point-of-Sale edits.



Anticipated Market Changes

Future patent expirations

- Nexium (esomeprazole) - 04/2014
- Prevacid (lansoprazole) - 05/2009
- Aciphex (rabeprazole) - 04/2009

Introduction of **Protonix® Delayed-Release Oral Suspension 40 mg**

- Protonix® Suspension contains enteric-coated granules of pantoprazole and can be administered orally in applesauce or apple juice, or mixed in apple juice through a nasogastric tube.
- Available in 40 mg unit dose packets.
- Comparison of cost of generic products as well as other products that can be administered through a nasogastric or PEG tube.

Cost Comparison

	EAC/ Unit	SMAC/ Unit	$/Month* (30 day supply)
Protonix ® (pantoprazole) Oral Suspension 40mg	$4.00		$124.15
Zegerid ® (omeprazole NaBicarb) 20-1680mg oral suspension	$5.10		$157.15
Zegerid ® (omeprazole NaBicarb) 40-1680mg oral suspension	$5.10		$157.15
Prevacid® (lansoprazole) Oral Suspension 15mg, 30mg	$5.31		$163.45
Pantoprazole tab 40mg		$2.85	$89.65
Pantoprazole tab 20mg		$2.97	$93.25
Omeprazole cap 40mg (two 20mg caps)		$0.37	$26.35
Omeprazole cap 20mg		$0.37	$15.25

*includes $4.15 dispensing fee. Costs do not include rebates.

Recommendations

The College of Pharmacy recommends placing Protonix® Oral Suspension in tier-2 of the Anti-ulcers PBPA Category. Approval requires specific reason why member cannot use available tier-1 products. Quantity limit of 30 packets for 30 days would also be applied.

Anti-Ulcer Medications

The following products requires prior authorization with a special reason for use:

- **ranitidine (Zantac) – effervescent tablets and capsules**
- **brand omeprazole 40mg (Prilosec 40mg caps)**

Tier 1	Tier 2
omeprazole (10 and 20 mg caps)	esomeprazole (Nexium Caps and I.V.)*
omeprazole/antacid (Zegerid Caps)	omeprazole/antacid (Zegerid Packets)*
lansoprazole (Prevacid) capsules	lansoprazole (Prevacid ODT and Granules)*
	pantoprazole sodium (Protonix Caps, Suspension and I.V.)*
	rabeprazole sodium (Aciphex Tabs)

Blue color indicates Supplemental Rebate Participation * Non-tablet dosage forms require reason for use.

Reference

1. Protonix Delayed-Release Oral Suspension® Product Information, Wyeth Pharmaceuticals, 5/2008. Available online at: http://www.wyeth.com/content/showlabeling.asp?id=135

Appendix G

Prior Authorization Annual Review FY08- Qualaquin®

Oklahoma HealthCare Authority
August 2008

Manufacturer	Mutual Pharmaceutical Company
FDA Classification	Antimalarial

Summary

Qualaquin®, the only FDA-approved quinine product available for the treatment of malaria, was approved in August 2005. Numerous products containing quinine sulfate were marketed without approved applications for malaria and many were used off-label to treat and/or prevent nocturnal leg muscle cramps and related conditions. However, on February 13, 2007 the FDA ordered all firms to cease manufacturing unapproved products containing quinine, including quinine sulfate products and any other salt of quinine due to the various adverse events associated with these products. Because of this, Qualaquin® is the only remaining FDA approved quinine product available on the market.

Prior Authorization Criteria

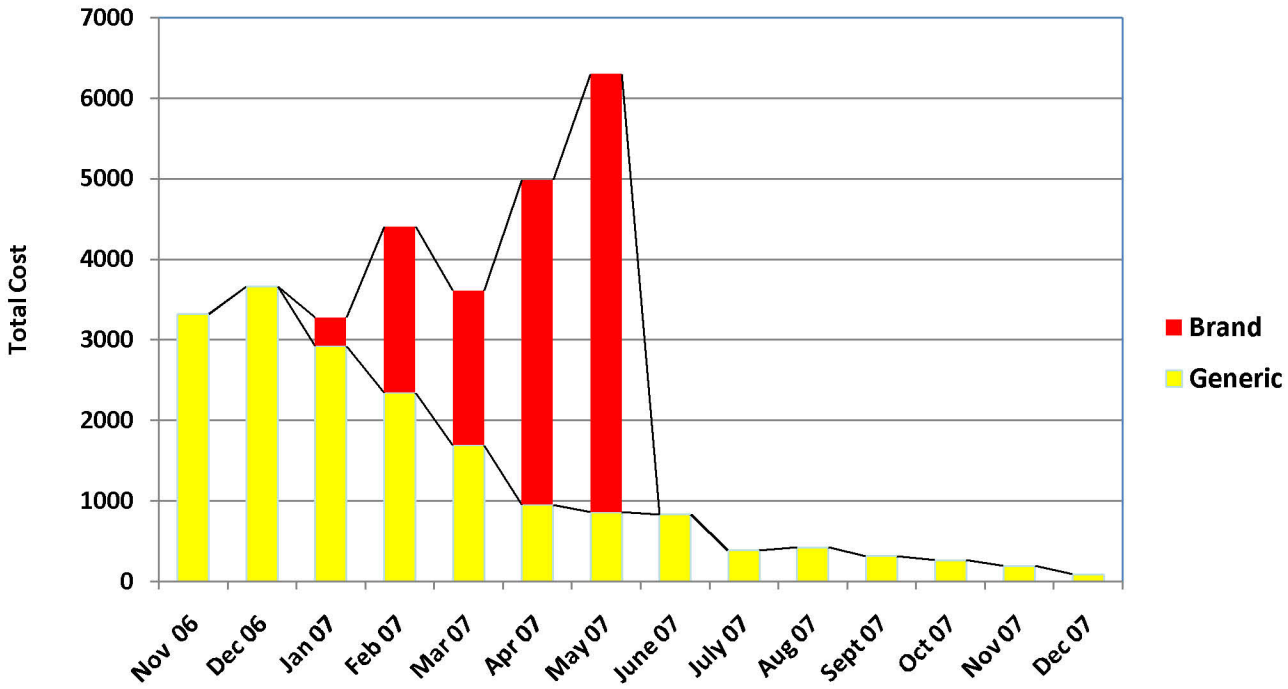
- Approval based on diagnosis of malaria.
- Off label use for the prevention/treatment of leg cramps and other related conditions will not be covered.

Approved in May 2007. Implemented June 1, 2007

Utilization – Fiscal Year 2007 vs. Fiscal Year 08

Total Cost FY '08	**$0**
Total Cost FY '07	*$13,806.65*
Total Claims FY '08	**0**
Total Claims FY '07	*75*
Total Clients FY '08	**0**
Total Clients FY '07	*48*
Per Diem FY '08	**$0**
Per Diem FY '07	*$4.79*

Qualaquin® Cost Trend



Prior Authorizations FY08

Prior Authorizations	No. of Petitions
Approved	0
Denied	52
Incomplete	2
Total	54

Recommendations

The College of Pharmacy recommends no changes at this time.

Appendix H

Bioequivalent Medications

August 2008

Introduction

Bioequivalent medications, often called generic drugs are identical, or bioequivalent to a brand name drug in dosage form, safety, strength, route of administration, quality, performance characteristics and intended use. The utilization of generic drugs has resulted in substantial savings to consumers and payers that range from $8 to $10 billion dollars annually. Although widely prescribed by doctors and recommended by pharmacists, some individuals have questions regarding the safety and efficacy of generic medications. The purpose of this paper is to address common questions regarding generic medications.

Approval Process of Innovator vs. Bioequivalent Medications

A "brand" name medication is the medication manufactured by the innovator pharmaceutical company. New drugs, like other new products, are developed under patent protection. The innovator company must submit a New Drug Application (NDA) and satisfy all components of the application in order to bring a new drug into the pharmaceutical market in the United States. The patent protects the manufacturer's investment in the drug's development by giving the innovator company the sole right to sell the drug during the patent period. When patents and regulatory periods of exclusivity expire, additional pharmaceutical manufacturers can submit an Abbreviated New Drug Application (ANDA) to market the "generic" version of the product. When those companies satisfy all components of the application, they are approved to manufacture and sell the "generic" version of the medication.

Below is a chart summarizing the two drug review processes.

NDA Requirements		ANDA Requirements
1. Labeling		1. Labeling
2. Pharmacology/Toxicology		2. Pharmacology/Toxicology
3. Chemistry		3. Chemistry
4. Manufacturing		4. Manufacturing
5. Controls		5. Controls
6. Microbiology		6. Microbiology
7. Inspection		7. Inspection
8. Testing		8. Testing
9. Animal Studies 10. Clinical Studies 11. Bioavailability Studies	⟺	9. Bioequivalence Studies

FDA approved generic drugs are manufactured by pharmaceutical companies that are required to meet the same rigid review process and manufacturing standards as the innovator drug companies.

Demonstration of Bioequivalence

Bioavailability refers to the rate and extent to which the active or therapeutic ingredient is absorbed from a drug product and becomes available at the site of drug action (Federal FD&C Act, section 505(j)(8)). **Bioequivalence** is defined as the absence of a significant difference in the rate and extent to which the active ingredient in two or more products becomes available at the site of drug action. Underlying the concept of bioequivalence is the premise that, if a drug product contains the same dose of a drug substance that is chemically identical and delivered to the site of action at the same rate and extent as another drug product, then the two products are bioequivalent and can be substituted or interchanged. Methods used to determine bioequivalence can be found in 21 CFR 320.24, and include:

1. Pharmacokinetic (PK) studies
2. Pharmacodynamic (PD) studies
3. Comparative clinical trials
4. In-vitro studies

The standard bioequivalence study is conducted using a two-treatment crossover study design in a limited number of healthy volunteers, usually 24 to 36 adults. Single doses of the test and reference drug products are administered and blood or plasma levels of the drug are measured over time. Pharmacokinetic parameters evaluated are:

Rate of absorption

- Measured by maximum or peak drug concentrations (Cmax)

Extent of absorption

- Measured by area under the plasma concentration-time curve (AUC), calculated to the last measured concentration (AUC(0-t)) and extrapolated to infinity (AUC(0-inf))

Generally, bioequivalence is demonstrated when the 90% confidence interval for both pharmacokinetic parameters (rate and extent of absorption) lies between the 80% to 125% boundaries. Other study designs include parallel, in-vitro, or equivalence studies with clinical or pharmacodynamic endpoints. Choice of study design used is based on the site of action of the drug and the ability of the study design to compare drug delivered to that site by the two products.

Post Approval Integrity of Bioequivalent Medications

Following approval, both generic and innovator companies must submit data to the FDA showing that their products continue to meet the agency's specifications until the established expiration date. Continued testing and inspections of the manufacturing facilities similar to that undergone by innovator drug companies assures the manufacturing facilities are in compliance with current Good Manufacturing Practices and Good Clinical Practices. These inspections are conducted primarily by field officers of the Office of Regulatory Affairs with support from the Office of Compliance and are assigned geographically. In addition, the FDA regularly assesses the use of generic medications on the market through researching and evaluating reports about their performance. A recent FDA review found that the average difference between the bioequivalence of more than 270 generic drugs approved in 1997 and their trade-name counterparts was 3.5 percent. This is about the same as the differences found between batches of trade-name products.

Suspected In-Equivalence

Suspected reports of inequivalence or any other adverse events pertaining to a medication can be reported to the FDA through Medwatch, which is available online at http://www.fda.gov/medwatch/. A Medwatch form is also included as Attachment A. In addition to public petitions received through Medwatch, the FDA also evaluates literature articles on therapeutic in-equivalence, reports from field officers, and congressional inquiries. These reports are reviewed and forwarded to the Associate Director of Medical Affairs and the following actions will be taken:

- Report is reviewed in-depth to determine if there are clinical concerns.
- Copy of report is forwarded to the Office of Drug Safety, if appropriate.
- Report is referred to the Associate Director for Chemistry if the matter appears to be solely a manufacturing product quality issue.
- Report is referred to the Therapeutic Inequivalence Action Coordinating Committee (TIACC) if the report presents evidence of the generic drug product not being equivalent to the reference listed drug or if it reports lack of effect of the generic drug.
- If report is reviewed and it is determined that no action is indicated, then that is documented.

The TIACC provides timely follow-up, and when appropriate, a full-scale investigation of therapeutic issues using a science-based process.

Conclusion

Bioequivalent medications make up roughly 70% of all prescriptions dispensed to SoonerCare members. Prior to release into the market these medications undergo a rigorous application and approval process by the FDA similar to the process for trade-name medications. In addition, FDA has provided control mechanisms to ensure high quality and performance of these medications similar to trade name medication monitoring. The FDA mandates these processes and control mechanisms to assure consumers that bioequivalent medications are therapeutically and clinically equivalent and can be confidently interchanged with their trade-name counterparts.

Reference:
United States Food and Drug Administration. **Office of Generic Drugs**. Available online at: http://www.fda.gov/cder/ogd/index.htm#Introduction

Attachment A

U.S. Department of Health and Human Services

MEDWATCH

The FDA Safety Information and Adverse Event Reporting Program

For VOLUNTARY reporting of adverse events, product problems and product use errors

Page ____ of ____

Form Approved: OMB No. 0910-0291, Expires:10/31/08
See OMB statement on reverse.

FDA USE ONLY
Triage unit sequence #

PLEASE TYPE OR USE BLACK INK

A. PATIENT INFORMATION — Section A - Help

1. Patient Identifier — In confidence
2. Age at Time of Event, or Date of Birth:
3. Sex — ☐ Female ☐ Male
4. Weight — ____ lb or ____ kg

B. ADVERSE EVENT, PRODUCT PROBLEM OR ERROR — Section B - Help

Check all that apply:

1. ☐ Adverse Event ☐ Product Problem *(e.g., defects/malfunctions)*
   ☐ Product Use Error ☐ Problem with Different Manufacturer of Same Medicine

2. Outcomes Attributed to Adverse Event *(Check all that apply)*
   ☐ Death: _____ *(mm/dd/yyyy)*
   ☐ Disability or Permanent Damage
   ☐ Life-threatening
   ☐ Congenital Anomaly/Birth Defect
   ☐ Hospitalization - initial or prolonged
   ☐ Other Serious (Important Medical Events)
   ☐ Required Intervention to Prevent Permanent Impairment/Damage (Devices)

3. Date of Event *(mm/dd/yyyy)*
4. Date of this Report *(mm/dd/yyyy)* 08/05/2008

5. Describe Event, Problem or Product Use Error

(Continue on page 2)

6. Relevant Tests/Laboratory Data, Including Dates

(Continue on page 2)

7. Other Relevant History, Including Preexisting Medical Conditions *(e.g., allergies, race, pregnancy, smoking and alcohol use, liver/kidney problems, etc.)*

(Continue on page 2)

C. PRODUCT AVAILABILITY — Section C - Help

Product Available for Evaluation? *(Do not send product to FDA)*

☐ Yes ☐ No ☐ Returned to Manufacturer on: _____ *(mm/dd/yyyy)*

D. SUSPECT PRODUCT(S) — Section D - Help

1. Name, Strength, Manufacturer *(from product label)*
   #1
   #2

2. Dose or Amount / Frequency / Route
   #1
   #2

3. Dates of Use *(If unknown, give duration) from/to (or best estimate)*
   #1
   #2

4. Diagnosis or Reason for Use *(Indication)*
   #1
   #2

5. Event Abated After Use Stopped or Dose Reduced?
   #1 ☐ Yes ☐ No ☐ Doesn't Apply
   #2 ☐ Yes ☐ No ☐ Doesn't Apply

6. Lot #
   #1
   #2

7. Expiration Date
   #1
   #2

8. Event Reappeared After Reintroduction?
   #1 ☐ Yes ☐ No ☐ Doesn't Apply
   #2 ☐ Yes ☐ No ☐ Doesn't Apply

9. NDC # or Unique ID

E. SUSPECT MEDICAL DEVICE — Section E - Help

1. Brand Name
2. Common Device Name
3. Manufacturer Name, City and State
4. Model # / Lot # / Catalog # / Expiration Date *(mm/dd/yyyy)* / Serial # / Other #
5. Operator of Device — ☐ Health Professional ☐ Lay User/Patient ☐ Other: _____
6. If Implanted, Give Date *(mm/dd/yyyy)*
7. If Explanted, Give Date *(mm/dd/yyyy)*
8. Is this a Single-use Device that was Reprocessed and Reused on a Patient? ☐ Yes ☐ No
9. If Yes to Item No. 8, Enter Name and Address of Reprocessor

F. OTHER (CONCOMITANT) MEDICAL PRODUCTS — Section F - Help

Product names and therapy dates *(exclude treatment of event)*

(Continue on page 2)

G. REPORTER — (Confidentiality statement) — Section G - Help

1. Name and Address
   Phone #
   E-mail
2. Health Professional? ☐ Yes ☐ No
3. Occupation
4. Also Reported to: ☐ Manufacturer ☐ User Facility ☐ Distributor/Importer
5. If you do NOT want your identity disclosed to the manufacturer, place an "X" in this box: ☐

U.S. Department of Health and Human Services

MEDWATCH

The FDA Safety Information and Adverse Event Reporting Program

(CONTINUATION PAGE)

For VOLUNTARY reporting of adverse events and product problems

Section B: 5. **Describe Problem or Product Use Error** ***(continued)***

Section B: 6. **Relevant Tests/Laboratory Data, Including Dates** *(continued)*

Section B: 7. **Other Relevant History, Including Preexisting Medical Conditions** *(e.g., allergies, race, pregnancy, smoking and alcohol use, liver/kidney problems dysfunction, etc.) (continued)*

Section F: **OTHER (CONCOMITANT) MEDICAL PRODUCTS - Product Names and Therapy Dates** *(Exclude treatment of event) (continued)*

General Instructions for Completing the MedWatch Form FDA 3500

For use by health professionals and consumers for **VOLUNTARY** reporting of adverse events, product use errors and product quality problems with:

- drugs
- biologics, (including blood components, blood derivatives, allergenics, human cells, tissues, and cellular and tissue-based products (HCT/Ps),
- medical devices (including *in vitro* diagnostics),
- combination products [e.g. drug-device, biologic-device]
- special nutritional products (dietary supplements, infant formulas, medical foods)
- cosmetics

Adverse events involving **vaccines** should be reported to the Vaccine Adverse Event Reporting System (VAERS), http://vaers.hhs.gov/pdf/vaers_form.pdf Adverse events involving **investigational (study) drugs, such as those relating to Investigational New Drug (IND) applications** should be reported as required in the study protocol and sent to the address and contact person listed in the study protocol. They should generally not be submitted to FDA MedWatch as voluntary reports.

Note for consumers: If possible, please take the 3500 form to your health professional (e.g., doctor or pharmacist) so that information based on your medical record that can help in the evaluation of your report will be provided. If, for whatever reason, you do not wish to have your health professional fill out the form, you are welcome to do so yourself.

GENERAL INSTRUCTIONS

- Please make sure that all entries are either typed, printed in a font no smaller than 8 point, or written using black ink.
- Please complete all sections that apply to your report.
- Dates should be entered as mm/dd/yyyy (e.g., June 3, 2005 = 06/03/2005). If exact dates are unknown, please provide the best estimate (see B3).
- For narrative entries, if the fields do not provide adequate space, attach additional pages as needed.
- If attaching additional pages, please do the following:
  - Identify all attached pages as *Page __ of __*
  - Indicate the appropriate section and block number next to the narrative continuation
  - Include the phrase continued at the end of each field that has additional information continued onto another page
- **Section D**, Suspect product[s], should be used to report on special nutritional products and cosmetics as well as drugs or biologics, including human cells, tissues, and cellular and tissue-based products (HCT/Ps).
- If your report involves a serious adverse event with a device and it occurred in a facility other than a doctor's office, that facility may be legally required to report to FDA and/or the manufacturer. Please notify the person in that facility who would handle such reporting.

QUESTIONS ABOUT VOLUNTARY REPORTING?

Call MedWatch at 800-FDA-1088 or 301-796-1935

ADVICE ABOUT VOLUNTARY REPORTING

Detailed instructions available at: http://www.fda.gov/medwatch/report/consumer/instruct.htm

Report adverse events, product problems or product use errors with:

- Medications *(drugs or biologics)*
- Medical devices *(including in-vitro diagnostics)*
- Combination products *(medication & medical devices)*
- Human cells, tissues, and cellular and tissue-based products
- Special nutritional products *(dietary supplements, medical foods, infant formulas)*
- Cosmetics

Report product problems - quality, performance or safety concerns such as:

- Suspected counterfeit product
- Suspected contamination
- Questionable stability
- Defective components
- Poor packaging or labeling
- Therapeutic failures (product didn't work)

-Fold Here-

Report SERIOUS adverse events. An event is serious when the patient outcome is:

- Death
- Life-threatening
- Hospitalization - initial or prolonged
- Disability or permanent damage
- Congenital anomaly/birth defect
- Required intervention to prevent permanent impairment or damage
- Other serious (important medical events)

Report even if:

- You're not certain the product caused the event
- You don't have all the details

How to report:

- Just fill in the sections that apply to your report
- Use section D for all products except medical devices
- Attach additional pages if needed
- Use a separate form for each patient
- Report either to FDA or the manufacturer *(or both)*

Other methods of reporting:

- 1-800-FDA-0178 -- To FAX report
- 1-800-FDA-1088 -- To report by phone
- www.fda.gov/medwatch/report.htm -- To report online

If your report involves a serious adverse event with a device and it occurred in a facility outside a doctor's office, that facility may be legally required to report to FDA and/or the manufacturer. Please notify the person in that facility who would handle such reporting.

-Fold Here-

If your report involves a serious adverse event with a vaccine call 1-800-822-7967 to report.

Confidentiality: The patient's identity is held in strict confidence by FDA and protected to the fullest extent of the law. FDA will not disclose the reporter's identity in response to a request from the public, pursuant to the Freedom of Information Act. The reporter's identity, including the identity of a self-reporter, may be shared with the manufacturer unless requested otherwise.

The public reporting burden for this collection of information has been estimated to average 36 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services
Food and Drug Administration - MedWatch
10903 New Hampshire Avenue
Building 22, Mail Stop 4447
Silver Spring, MD 20993-0002

Please DO NOT RETURN this form to this address.

OMB statement:
"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number."

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

FORM FDA 3500 (10/05) (Back) **Please Use Address Provided Below -- Fold in Thirds, Tape and Mail**

DEPARTMENT OF
HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

Official Business
Penalty for Private Use $300

NO POSTAGE
NECESSARY
IF MAILED
IN THE
UNITED STATES
OR APO/FPO

BUSINESS REPLY MAIL
FIRST CLASS MAIL PERMIT NO. 946 ROCKVILLE MD

MEDWATCH
The FDA Safety Information and Adverse Event Reporting Program
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20852-9787

Appendix I

Follow Up to the January 3, 2008 Communication About an Ongoing Safety Review Erythropoiesis-Stimulating Agents (ESAs) Epoetin alfa (marketed as Procrit, Epogen) Darbepoetin alfa (marketed as Aranesp)

This information reflects FDA's current analysis of available data concerning these drugs. FDA intends to update this document when additional information or analyses become available.

On April 22, 2008, FDA notified the manufacturer of Epogen/Procrit and Aranesp of its decision to require additional safety-related changes to the labeling for these products.

Amgen submitted labeling supplements for Epogen/Procrit and Aranesp on May 22, 2008, following the March 13, 2008 Oncologic Advisory Committee's recommendations to make additional safety-related changes to the labeling for these products. Amgen and FDA have agreed on many of these changes, including to replace the existing Patient Package Insert with a Medication Guide and to modify certain sections of the Boxed Warnings, Indications and Usage, and Dosage and Administration sections of package insert.

These changes are intended to clarify the FDA-approved conditions for use of ESAs in patients with cancer and revise directions for dosing to state the hemoglobin level at which treatment with an ESA should not be initiated. While agreement was reached on the general concepts, Amgen and FDA have not reached agreement on specific wording on two points, including a warning statement that ESAs are not intended for use in patients receiving myelosuppressive therapy when the expected outcome is cure and statements regarding when to initiate and to discontinue ESA dosing. Labeling discussions concluded on July 15 and FDA issued a letter ordering the additional changes on July 30, 2008.

FDA's action to require these safety labeling changes follows the completion of the review of information received in November 2007 and December 2007 and are in keeping with the recommendations made at the March 13, 2008 Oncologic Drugs Advisory Committee meeting. Amgen has been ordered to make the additional changes under new authorities provided in the FDA Amendments Act of 2007 and has 5 days to appeal or 15 days to submit a supplement containing the labeling changes.

FDA continues to encourage healthcare professionals to discuss with their patients before starting or continuing therapy with ESAs, the benefits of treatment with ESAs and the potential and demonstrated risks of ESAs for thrombovascular events, shortened time to tumor progression or recurrence, and shortened survival time.

The FDA urges healthcare professionals to promptly report serious and unexpected adverse reactions associated with Epogen, Procrit and Aranesp to the FDA MedWatch reporting program, as described below.

- online at www.fda.gov/medwatch/report.htm
- by returning the postage-paid FDA form 3500 (available in PDF format at www.fda.gov/medwatch/getforms.htm) to 5600 Fishers Lane, Rockville, MD 20852-9787
- faxing the form to 1-800-FDA-0178
- by phone at 1-800-332-1088

Information for Healthcare Professionals

Fluoroquinolone Antimicrobial Drugs [ciprofloxacin (marketed as Cipro and generic ciprofloxacin), ciprofloxacin extended release (marketed as Cipro XR and Proquin XR), gemifloxacin (marketed as Factive), levofloxacin (marketed as Levaquin), moxifloxacin (marketed as Avelox), norfloxacin (marketed as Noroxin), and ofloxacin (marketed as Floxin and generic ofloxacin)]

FDA ALERT [7/8/2008]: FDA is notifying the makers of fluoroquinolone antimicrobial drugs for systemic use of the need to add a boxed warning to the prescribing information about the increased risk of developing tendinitis and tendon rupture in patients taking fluoroquinolones and to develop a Medication Guide for patients. The addition of a boxed warning and a Medication Guide would strengthen the existing warning information already included in the prescribing information for fluoroquinolone drugs.

Fluoroquinolones are associated with an increased risk of tendinitis and tendon rupture. This risk is further increased in those over age 60, in kidney, heart, and lung transplant recipients, and with use of concomitant steroid therapy. Physicians should advise patients, at the first sign of tendon pain, swelling, or inflammation, to stop taking the fluoroquinolone, to avoid exercise and use of the affected area, and to promptly contact their doctor about changing to a non-fluoroquinolone antimicrobial drug.

Selection of a fluoroquinolone for the treatment or prevention of an infection should be limited to those conditions that are proven or strongly suspected to be caused by bacteria.

This information reflects FDA's current analysis of data available to FDA concerning fluoroquinolone antimicrobials. 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 fluoroquinolone antimicrobials, please contact the FDA MedWatch program and complete a form on line at http://www.fda.gov/medwatch/report/hcp.htm or report by fax to 1-800-FDA-0178, by mail using the postage-paid address form provided on line, or by telephone to 1-800-FDA-1088.

FDA is notifying the makers of fluoroquinolone antimicrobial drugs of the need to add a *Boxed Warning* to the prescribing information about the increased risk of tendinitis and tendon rupture in patients taking fluoroquinolones and to develop a Medication Guide for patients.* Fluoroquinolone antimicrobial drugs are used to treat various bacterial infections. Marketed fluoroquinolone antimicrobial drugs include ciprofloxacin (marketed as Cipro and generic ciprofloxacin), ciprofloxacin extended release (Cipro XR and Proquin XR), gemifloxacin (marketed as Factive), levofloxacin (marketed as Levaquin), moxifloxacin

FDA News

FOR IMMEDIATE RELEASE
July 9, 2008

Media Inquiries:
Christopher DiFrancesco, 301-827-6242
Consumer Inquiries:
888-INFO-FDA

FDA Revises Process for Responding to Drug Applications

The U.S. Food and Drug Administration today announced that it is revising the way it communicates to drug companies when a marketing application cannot be approved as submitted.

Under new regulations that govern the drug approval process, FDA's Center for Drug Evaluation and Research (CDER) will no longer issue "approvable" or "not approvable" letters when a drug application is not approved. Instead, CDER will issue a "complete response" letter at the end of the review period to let a drug company know of the agency's decision on the application.

"These new regulations will help the FDA adopt a more consistent and neutral way of conveying information to a company when we cannot approve a drug application in its present form," said Janet Woodcock, M.D., director of the agency's Center for Drug Evaluation and Research (CDER). "Thorough and timely review of drug applications is a priority of the FDA, and these new processes will make our communications with sponsors of applications more consistent."

Taking the place of "approvable" and "not approvable" letters, a "complete response" letter will be issued to let a company know that the review period for a drug is complete and that the application is not yet ready for approval. The letter will describe specific deficiencies and, when possible, will outline recommended actions the applicant might take to get the application ready for approval.

Currently, when assessing new drug applications, the FDA can respond to a sponsor in one of three types of letters: an "approval" letter, meaning the drug has met agency standards for safety and efficacy and the drug can be marketed for sale in the United States; an "approvable" letter, which generally indicates that the drug can probably be approved at a later date provided that the applicant provides certain additional information or makes specified changes (such as to labeling); or a "not approvable" letter, meaning the application has deficiencies generally requiring the submission of substantial additional data before the application can be approved.

"Complete response" letters are already used to respond to companies that submit biologic license applications. The process for drugs and biologics will be consistent under the new regulations.

The revision should not affect the overall time it takes the FDA to review new or generic drug applications or biologic license applications. These changes, which will become effective on Aug. 11, 2008, are not expected to directly affect consumers.

In July 2004, the FDA issued a proposed rule on these topics. At that time the agency asked for comments on the proposal. Today's final rule addresses comments submitted to the agency.

For more information, see:

Link to the Complete Response Final Rule
http://www.fda.gov/cder/regulatory/complete_response_FR/default.htm

Link to the drug approval process page
http://www.fda.gov/fdac/special/testtubetopatient/default.htm