THE UNIVERSITY OF OKLAHOMA

MEMORANDUM

TO: Drug Utilization Review Board Members

FROM: Ron Graham, D.Ph.

SUBJECT: **Packet Contents for Board Meeting – September 14, 2004**

DATE: September 8, 2004

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

Enclosed are the following items related to the September 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 – Discuss and Vote on Prior Authorization of Fuzeon™- **See Appendix C.**

Review and Discuss Xopenex™ Utilization - **See Appendix D.**

Review and Discuss Hepatitis C Agents Utilization - **See Appendix E.**

Review and Discuss Restasis™ Utilization - **See Appendix F.**

Review and Discuss Anti-Emetic Utilization – **See Appendix G.**

Review and Discuss Regranex™ Utilization – **See Appendix H.**

Review and Discuss Colony Stimulating Factor Utilization – **See Appendix I.**

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

Future Business

Adjournment

PRELIMINARY COURTESY AGENDA
FINAL AGENDA POSTED 24 HOURS IN ADVANCE OF MEETING

Drug Utilization Review Board

(DUR Board)

Meeting – September 14, 2004 @ 6:00p.m.

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

AGENDA

Discussion and Action On the following Items:

Items to be presented by Dr. Whitsett, Chairman:

1. Call To Order

A. Roll Call – Dr. Graham

Items to be presented by Dr. Whitsett, Chairman:

2. Public Comment Forum

A. Acknowledgment of Speakers and Agenda Item

Items to be presented by Dr. Whitsett, Chairman:

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

A. July 13, 2004 DUR Minutes - Vote
B. Memorandum of August 2, 2004
C. Provider Correspondence

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

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

A. Therapy Management Quarterly Update
B. Retrospective DUR Report for May / June 2004
C. Medication Coverage Activity Audit for July / August 2004
D. Help Desk Activity Audit for July / August 2004

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

5. Action Item – Discuss and Vote on Prior Authorization of Fuzeon™- See Appendix C.

A. Utilization Review
B. COP Recommendations

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

6. Review and Discuss Xopenex™ Utilization – See Appendix D.

A. Utilization Review
B. COP Recommendations

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

7. Review and Discuss Hepatitis C Agents Utilization – See Appendix E.

A. Utilization Review
B. COP Recommendations

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

8. Review and Discuss Restasis™ Utilization – See Appendix F.

A. Utilization Review
B. COP Recommendations

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

9. Review and Discuss Anti-Emetic Utilization – See Appendix G.

A. Utilization Review
B. COP Recommendations

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

10. Review and Discuss Regranex™ Utilization – See Appendix H.

A. Utilization Review
B. COP Recommendations

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

11. Review and Discuss Colony Stimulating Factor Utilization – See Appendix I.

A. Utilization Review
B. COP Recommendations

12. FDA and DEA Updates – See Appendix J.

13. Future Business

A. RA Medications Review
B. Antidementias Review
C. Benzo/Ambien™ Follow-up Review
D. Growth Hormones Review
E. Neurontin™ Follow-Up Review
F. MS Copolymers Review
G. Supplemental Rebate Update
H. Narcotic Analgesic Review

14. Adjournment

APPENDIX A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of JULY 13. 2004

BOARD MEMBERS:	PRESENT	ABSENT
Rick G. Crenshaw, D.O.		X
Dorothy Gourley, D.Ph.	X	
Cathy Hollen, D.Ph.		X
Dan McNeill, Ph.D., PA-C	X	
Cliff Meece, D.Ph.	X	
Dick Robinson, D.Ph., Vice-Chair	X	
James M. Swaim, D.Ph.	X	
Thomas Whitsett, M.D., Chair		X
(VACANT)		NA
(VACANT)		NA

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

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Kristall Bright; Pharmacy Financial Analyst		X
Alex Easton, M.B.A.; Pharmacy Operations Manager	X	
Mike Fogarty, C.E.O	X	
Lynn Mitchell, M.D., M.P.H, Medical Director	X	
Nancy Nesser, D.Ph., J.D.; Pharmacy Director	X	
Howard Pallotta, J.D.		X
Lynn Rambo-Jones, J.D.	X	
Rodney Ramsey; Pharmacy Claims Specialist	X	

OTHERS PRESENT:

Geoff Holt, Pfizer
Jonathan Klock, GSK
John Omick, Novartis
Robert Hasselman, Wyeth
Jill Miller, TAP
Patrick Gotcher, BMS
Angela Menchaca, Amgen
Rod Woods, Medimmune
Cindy Brueke, Novartis
Vicki Macios, CVMS
Chris Sholer, Seel
Sandy Ruble, Seel
Rob Wiewel, Sanofi-Synthelabo
Loren Jordan, Medimmune
Lenn Stewart, Merck
Patrice Aston, DO
Anne Cuccio, MD; Mental Health Assoc.
Toby Thompson, Pfizer
Diana Moraseh, AstraZeneca
Greg Novarro, Sepracor
Joe McIntosh, Novartis
Adri Bornman, Novartis
Tim Myers, Schering-Plough
Rhonda Olsen, GSK
Curtis Krause, Medimmune
Cindy Flesher, BMS
Susan Schwarz, CVMS
Holli Hill, Sankyo Pharma
Ron Schnare, Abbott
Kay Kaut, Amylin
Scott Johnson, Pfizer
Holly Jacques, Merck
Vince Morrison, Forest
Lenora Crockett, BMS
Barbara Boner, Novartis
JoAnne Hargraves, Schering
Matt Johnson, Takeda
Rhonda Clark, Purdue
Connie Lindsey, AstraZeneca
John Bradshaw, GSK
Mark DeClerk, Lilly
Becky Alderson, BMS
Candie Phipps, Boehringer-Ingelheim
Charlene Kaiser, Wyeth
Randy McGinley, Berlex
S. Thompson, GSK
Christi Davis O'Brien, AstraZeneca
Tim Froley, Pfizer
Darryl Kabils, MD; SW Med. Ctr.

PRESENT FOR PUBLIC COMMENT:

Dr. Michelle Ware, St. Anthony's	Agenda Item No. 6
David McElwain, Outpatient Psych., Tulsa	Agenda Item No. 6
Alan Mason, OmniCare	Agenda Item No. 6
Evie Knisely, Novartis	Agenda Item No. 7
Dr. David Browning, Sanofi	Agenda Item No. 7
Chris Sholer, physician	Agenda Item No. 7
Mat Kumar, AstraZeneca	Agenda Item No. 7
Dr. Jason Sigmon, BMS	Agenda Item No. 9

AGENDA ITEM NO. 1: CALL TO ORDER

1A: Roll Call

Dr. Robinson called the meeting to order. Roll call by Dr. Graham established the presence of a quorum.

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 2: PUBLIC COMMENT FORUM

2A: Acknowledgement of Speakers and Agenda Item

Dr. Robinson acknowledged Public Comment speakers as noted above.

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 3: APPROVAL OF DUR BOARD MINUTES

3A: Corrected May 11, 2004 DUR Minutes

Corrected minutes submitted in agenda packet.

3B: June 8, 2004 DUR Minutes

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

ACTION: MOTION CARRIED.

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

4A: Prospective DUR Report: CMS Annual Report

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

4B: Retrospective DUR Report: March/April 2004

Responses from January/February follow-up were: January – 57% pharmacies, 61% physicians; February – 54% pharmacies, 31% physicians. Duplicate benzodiazipine therapy (female); March 2004: total responses were 52% pharmacies, 31% physicians. Duplicate benzodiazipine therapy (male); April 2004: total responses were 43% pharmacies, 7% physicians. Materials included in agenda packet; presented by Dr. Flannigan.

4C: Medication Coverage Activity Report: June 2004

The June 2004 activity audit noted total number of petitions submitted was 16,454 including super-PA's and special circumstance PA's. Approval/denial/duplicate percentages were indicated on the reports included in the agenda packet for this meeting. Monthly reports included in agenda packet; presented by Dr. Browning.

4D: Help Desk Activity Report: June 2004

Total calls for June 2004 numbered 16,634 (85.7% pharmacies, 7.9% clients, 2.4% physicians, 4.0% other). Monthly reports included in agenda packet; presented by Dr. Browning.

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 5: DISCUSS & VOTE ON PRIOR AUTHORIZATION OF SYNAGIS™

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

Dr. McNeill: *The use of multiple doses for multiple children from the same single vial was brought to my attention by a citizen of the state. Under D on page 63 of the packet it states that multiple patients are not to be treated from a single vial. The Health Care Authority has a quality assurance committee to monitor this practice. I'm comfortable with that.*

Dr. Gourley moved to prior authorize Synagis™; motion seconded by Dr. Meece. **7**

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 6: DISCUSS & VOTE ON PRIOR AUTHORIZATION OF SSRIs

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

For Public Comment, Dr. Michelle Ware: *I would like to speak to the issue of having prior authorization for SSRIs. I understand there is a call to have a restricted formulary with different tiers and that the proposed tier right now is for first tier to be the available generics that are warranted, and I actually have several letters that have been written to, I don't know if you've had access to those, and one of the letters that was written has actually been signed by 600 clinicians across the state, so and a lot of the information that I'm going to share with you was in this letter concerning the SSRIs in general and really, I guess my first point is, I want to talk just about, yes . . .*

Dr. Nesser: *I have a question about how those signatures were gathered, who did, who did the legwork for that?*

Dr. Ware: *You know, I'm not sure. Dr. Chesler wrote the letter. I signed it. I work with Dr. Chesler, so . . .*

Dr. Nesser: *Who, who asked you to sign it?*

Dr. Ware: *Dr. Chesler. I work with him at St. Anthony's.*

Dr. Nesser: *All right. We, we called a couple of physicians on there and it was, it was not Dr. Chesler who went around and gathered these 600 signatures. They were from across the state and they were carried into the offices by a pharmaceutical representative. So I think that should be make clear, that these were not, these were not just submitted by the physicians. They were, they were sought out . . .*

Dr. Ware: *That's correct, but they did sign agreeing with the information that was in the letter. I mean, I saw the letter. I would not have signed it had I not agreed with it.*

Dr. Nesser: *Okay, I just want to make sure that everyone knows where those signatures came from.*

Dr. Ware: *That's fine. Which makes sense because, you know, there's some people that are in a lot of offices around the state.*

Dr. Nesser: *Exactly.*

Dr. Ware: *Exactly. But anyway, so the point I would like to make is the whole premise of even have a restricted formulary would be that the SSRIs are all the same. And I would like to really, to really say that is not true. The SSRIs are very different, and if you look at the reasons for this, they are the same in that they are SSRIs, they're selective serotonin reuptake inhibitors, that's true. They are alike in that they do not cause death and overdose. There's no toxicity with overdose, that is how they're the same, but they're actually very different in the chemical structure based both on efficacy and side effects. If, I mean you talk to any clinician that uses the medications, you can have one patient be on three different SSRIs. They will respond to one and not two others. If they were exactly the same medication, we would have the same response. We would have the same side effect profiles, and they're not. They're very different. And in the letters that you read, Dr. Cranmer actually wrote a letter. He deals with the elderly, and he makes some very good points about the pharmacokinetics of the medications and that there is a lot of drug interaction, and actually if you look at the pharmacokinetics of these medications, the three that are proposed to be on the formulary have the highest incidence of inhibiting the systems where many of our medications are cleared through the liver. And what happens that they inhibit these systems, these cytochrome P450 systems in the liver you get an elevation of any other medications that the patient may be on. Some medications actually can cause toxicity and death. So, and of the three that are left on the formulary, those are the worst offenders. The other thing is that shows these medications are not the same, is if you don't just look at serotonin effects, but if you look at norepinephrine, dopamine, there is a reception called the sigma receptor. We don't even know the function of that. But we do know that there are different binding affinities for all of these receptors. They're different. They're different drugs, they have different effects. The second, which I understand cost is a huge issue, but you know I'm a taxpayer, I understand we have to keep costs down. Last year I had a quite lengthy conversation with Dr. Fogarty who used to be Medical Director for Heartland HMO. I do treat a lot of Medicaid patients and I talked with him about cost at the time because they were making formulary restrictions at that time, and I had shared with him at the time of some cost saving techniques that I thought we could use, just with the medications themselves. Education. You know, one of the things that's important, some of the medications you can write higher doses, split them in half and get two days' worth of medication for one day's price. And these are things that I'm not sure that all doctors are educated on. I think most psychiatrists are aware of these factors, because we use them a lot, but a lot of these medications are being prescribed by primary care physicians and people who may not have access to as much of*

this information about cost comparisons and what can be done to save. So these are things that I can certainly would help with the cost. That's just with direct medication cost. I think in the bigger picture, that is just a small piece of the price that we pay for mental health treatment in the state. I'm getting close, okay. We not only have the medication cost, we have hospitalization. If we're too restricted and we're not able to treat for a specific population, we're going to have increased morbidity and mortality, increased hospital days. One . . the cost of one hospital day would pay for months of medication treatment. You know. So in the scheme of things I think the cost of medications is just a small portion that we really need to look at the whole picture and not individually. So, allright, I don't have too much longer. I think the, probably the most important thing that I would like to suggest is that when you look at the indications on these medications, because I know that's been one of the arguments, Paxil treats anxiety disorders, Prozac treats major depressive disorder, and Luvox treats obsessive compulsive disorder, but the problem is, is these indications that we have with these research protocols, research protocols are very specific. Anyone that has anything to do with research protocols we know the patient, in order to enter protocol has to be what we call very clean. They can have nothing else going on. They just have to have a single disorder. They have no medical illnesses. They have to have nothing extraneous that would jeopardize the validity of the research protocol. And this is not what we see in practice. Most of my patients, I could never put into a clinical trial. Thank you. Any questions?

Dr. Graham: *I have one question. Have you prescribed Prozac and Luvox and Paxil before?*

Dr. Ware: *Yes I have.*

Dr. Nesser: *Have you prescribed them as your first choice?*

Dr. Ware: *Yes I have.*

Dr. Nesser: *And what would make them not your first choice?*

Dr. Ware: *What would make them not my first choice? Okay. First of all when we talk about Prozac, we have to talk about brand name versus generic because there is a difference. Within the first two months of changing from the brand name to generic, I had, I can't remember. There were many patients that I can just think off the top of my head that relapsed. Because the problem with generics is that they're not the same as brand. There can be a 20% variance, lower or higher.*

Dr. Nesser: *Okay. We're all hip to that. That's not going to . . We're good with that.*

Dr. Ware: *You understand that, okay. Yeah. I mean really it depends on the patient profiling and you know, which patients are best you know for each medication.*

Dr. Nesser: *Do you understand how this would work . . . how our step therapy program would work?*

Dr. Ware: *Yes, I did read the proposal. Yeah. Yes I did.*

Dr. Nesser: *Okay. Allright.*

Dr. Graham: *My question is, so you're really concerned about the generic versus the brand more than you are the choice of the drugs?*

Dr. Ware: *Well, not necessarily. No, not necessarily. I think, I think what I'm most concerned about is the limitation. You know I treat mostly children and adolescents. There is one drug on that formulary that I will be able to use, and that's Prozac. And that is, I mean, you know, the hundreds of patients that I treat, and I'm only going to be able to use one SSR, I mean, why, I kind of feel like, you know, what am I doing, you know. It's not up to me to decide what is best for this patient that I know. That I have analysis, that I've been seeing for months, years and I've gotten to know the family circumstances. I know everything about them, and I have only one SSRI to use. I think, you know, that's not the practice of medicine to me.*

Dr. Nesser: *And you understand that we're not going to . . . they're not going to be knocked off their medicine that they're on now. They'll be able to stay on whatever they're on now. You understand that?*

Dr. Ware: *I do understand that, but then I also understand that even future patients, when I'm seeing them for the first time, that I can guarantee that many of them I'm not going to find those medications as my first choice. Some of them I will, and that's why I say we need to educate. Because if I have a patient that I don't really, there's no reason to really go toward one or the other, you know I would love to see the cost comparisons and have it in my office and say well, you know what, it really doesn't matter which one this patient's on. The cheapest one is this one, you know, I think we need to form an alliance, really, in looking at that, because I am interested in saving money. I mean, you know, I'm not trying to be frivolous in saying well this is what I think is going to be maybe the most expensive, but too bad. Well, no. You know, it's got to be very specific for me what I choose depending on the patient. And this is going to make it very difficult and I think it's going to be harmful for a lot of my patients.*

Dr. Nesser: *Do you understand that the manufacturers have the opportunity to offer supplemental rebate so that their product is cost effective, the same as the products on Tier I and so that if they will make their products equivalent in cost, they will also be available without prior authorization?*

Dr. Ware: *And we physicians are caught in the middle.*

Dr. Nesser: *Right. I mean you see those guys more than we do, the manufacturer, so . . .*

Dr. Ware: *I know. And there is two sides to that, you know. I mean you could argue that going both ways, but you know, I'm just here saying that from a physician's standpoint . . .*
Dr. Nesser: *Right. We appreciate you coming.*
Dr. Gourley: *Can I ask you one more question about generic versus brand? We've had people come in and consistently say generics are crap. There is a method of reporting therapeutic failure. If you feel that a drug is inferior, then you should file a MedWatch report and let the FDA investigate that particular drug. And if that particular drug is inferior, it'll be removed from the market.*
Dr. Ware: *Well, I think the biggest problem with the generics when it comes to the SSRIs is that when the pharmacies order generics, they don't order from the same company every time, and every company has different variability with the amount of drug, and it can be up to like I said, a 40% difference, so if one month they're getting from this supplier, the next time they're getting . . .*
Dr. Swaim: *Slow down. No.*
Dr. Ware: *You know, it's a possibility. I'm not saying that it's going to happen every time, but it is, it is a possibility.*
Dr. Gourley: *Well, they have to meet FDA standards. The pharmaceutical manufacturers, whether it be generic or brand name have to meet FDA standards . . .*
Dr. Ware: *Which is up to 40% variance, correct . . . which is a 40% . . .*
Dr. Nesser: *It's not, it's not 40%.*
Dr. Ware: *It's 20% more or 20% less.*
Dr. Nesser: *But that's for the brand name, too, from batch to batch. It's the same for brand and generic.*
Dr. Graham: *It's all the same. It's the same . . same standard.*
Dr. Nesser: *It's all the same.*
Dr. Ware: *But at least, you know, you're getting from the same manufacturer. I mean, I don't know you know. All I know is I can tell you from my clinical experience that when the medication went to generic, I had some significant problems.*
Dr. Gourley: *Then you should . . . the FDA. You know, you should have, you should have filed a MedWatch report, you should have gone back to the pharmacist and said "I've had a therapeutic failure". I mean, that's the only way to address that, because if that's really true that the drug is inferior in the generic form then it should be off, it needs to be gone. You know, so . . .*
Dr. Robinson: *In going along with what Dr. Ware is saying, it might be something useful to put it in our educational letter to the state providers.*
Dr. Graham: *That's a good point.*
Dr. Ware: *It may be to just, all from one manufacturer.*
Dr. Robinson: *Or to at least address how to resolve the problem. Dr. Ware, thank you.*
For Public Comment, Alan Mason: *My name's Alan Mason and I practice geriatric pharmacy so the only thing I'm going to be talking about is geriatrics. And they mentioned Sequoia because I've been in that same building for 20 years, but I'm actually Regional Clinical Director with OmniCare and I'm responsible for all clinical interventions in about ten states. I'm founder and past president of the Oklahoma American Society of Consultant Pharmacy, state chapter, and I also represent Garrett Huxel, the president-elect couldn't make it today. I'm also a past board member of the national organization of the American Society of Consultant Pharmacy. And so with that being said, I want to talk and represent the elderly that I serve. One of their main things I want to talk about is the endemic nature of depression in the elderly. Thirty percent of people in long term care are depressed. Ten percent in the community are depressed. It's easy to say, well you'd be depressed too if you're in a nursing home, that's what I'm going to say, but the reality of it is the reason those people are there is because we have an increased amount of dementia and Alzheimer's disease. Those syndromes create an increased amount of depression. Also, one of the things that we need to appreciate as we age, we just don't get to be older adults. Our physiology changes. An elderly person's physiology is as much a different as a pediatric person's from an adult. Because of that, we have to take special considerations into account. And not only that, but we have to do that with drug selection. The reason I came today, I heard about this at the last minute. I'm sorry to say I really didn't know about it, but it was important to me so I came because the SSRI class is one of the few classes that we actually, we do it all the time, but it is every, everybody agrees that all these drugs are pretty much efficacious. They will work. However, what we're choosing for the elderly, we all choose them by side effect profile. And as the previous speaker was alluding to, all the side effect profiles are different. And because of the side effect profiles, the ones in Tier II are the first line drugs that we use in the elderly. The side effect profiles on the ones on Tier I have much more side effects, have longer durations of action in the frail elderly. The average age a person I talk with is 85 years of age. So they are not as, they're just not great drugs. Also if you look at the literature, the newer drugs have the most geriatric literature. Most of the drugs have no geriatric literature, so we have to extrapolate and make educated decisions on that. So because of these differences and the side effect profiles, one of the things we have to look at is anticholinergic load. The*

average elderly person, a lot of times in the present state they're overly, they're on a lot of drugs. They are. And the reason they are is because we treat chronic disease, and chronic disease starts at age 45. Those people start with arthritis and chronic heart failure and things like that. With the side effect profiles, especially anticholinergic side effects, you'd get an additive side effect profile which in the elderly, can be detrimental to their quality of life and their activities of daily living; particularly they will cause a decrease in cognition, increase in urinary retention, constipation which is something that is one of the primary things for causing delirium, and often times when this delirium isn't sought out or recognized, they get put on an antipsychotic "illegible". So it is important to keep them on the lowest side effect drugs as possible. For a lot of these reasons that I've kind of went through and it, you can just expand, but I know I've got a limited amount of time, our recommendation from the Amercian Society of Consultant Pharmacy, Oklahoma Chapter, is the same as when I first met this group on the review before when they were looking at doing the same thing with the benzodiazepines. But because we stated our case and the differences that we're looking at, we'd like you to consider excluding the elderly from this initiative. The reason for that is when you look at the numbers, it's not as big a percentage as you'd think. Only 10% of the elderly nationwide are in long term care. Thirty percent of that 10% are depressed. That means 90% of the elderly at home and only 10% of the 90% are depressed. By picking the best drug at the best time, you're going to keep adverse reactions from happening. One of the things that can happen with this as well as hypertension, you can actually get falls and get fractures and then you're in a nursing home. Fifty percent of all hip fractures die before the first year. So these are some of the issues that we deal with on a daily basis and we appreciate your consideration.

Dr. Swaim: *I was just going to say, you're talking in some generalities. What's your drug of choice that you want moved?*

Dr. Mason: *I use a lot of Zoloft, I use a lot of Celexa because as the prior speaker said, 70% of the people will respond to one drug. That means 30% won't because there are differences and we can't predict those differences.*

Dr. Swaim: *So your first line would be Zoloft?*

Dr. Mason: *Or Celexa. Now actually when you're asking me, I'll take the . . .*

Dr. Swaim: *Yeah, because we don't have a lot of choices here you know.*

Dr. Mason: *I'd take Lexapro over Celexa because Lexapro does have a cleaner side effect profile and the whole arm versus left arm thing, you know, some people look at it that I actually believe it and we've done a lot of it, we've seen good effects with that.*

Dr. Gourley: *One question had to do with the provider status. Do you provide the drugs to your patients? I mean is that part of what your company does, or . . .?*

Dr. Mason: *My company is a pharmacy provider and we have kind of like two arms if you think . . . we have an institutional pharmacy side which means that we only service nursing home patients.*

Dr. Gourley: *So you're closed door pharmacies.*

Dr. Mason: *So we're closed door pharmacy. However, on the other side, where I'm Regional Director, I'm in charge of consultant pharmacists that are in patients charts interacting with physicians all the time, interacting with nurses all the time, interacting with patients all the time. And so my job is to help them have tools and make the best clinical decisions possible.*

Dr. Gourley: *As a closed door pharmacy, are you eligible to belong to purchasing organizations and receive reduced pricing on drugs?*

Dr. Mason: *I don't know about that because I'm only involved in clinical issues. I do know that we're the largest closed door pharmacy in the United States.*

Dr. Gourley: *So you would assume that price negotiations would be a part of that?*

Dr. Mason: *I assume that we have good price negotiations, but . . .*

Dr. Gourley: *Do you have any kind of restrictions, formulary restrictions or anything like that that you impose within your organization?*

Dr. Mason: *No, there's no restrictions. We have open . . . it's an open formulary. We do have, we have taken the time and considerable money to develop a guideline which we call a geriatric pharmaceutical care guideline, which is developed to identify by scientific literature the best choice for the elderly. But with that, if I'm talking to a physician, put it this way. My mom just had a coronary bypass, one of the things that are common with coronary bypass patients is depression. She is depressed. She's on Celexa. If she couldn't have got that, I'd have been comfortable going with Zoloft, but I chose those because I feel those are the best things for the elderly and as a rule I never do anything for my patients I don't do for myself.*

Dr. Graham: *Alan, I want to thank you for coming. We appreciate what you're saying. I've got a question, though. You say one of your goals I think, is to get the best drug at the best time for your patients in the elderly population, especially in the nursing home. How do you guys respond when you see all these atypical uses going on, and compared to SSRI use which you're telling us you have preferences over that, but why would you not recommend changing a lot of these people from atypicals to SSRIs?*

Dr. Mason: *Okay, the reason I said that is because that is one of the areas of interest for me. I spoke to the Oklahoma Medical Directors Association on that topic and just last week, I just spoke to the Texas Pharmaceutical Association; combative behaviors in the elderly, how to deal with pharmacotherapy. It's, as a rule, you want to use the drug that is best situated for the event and in the elderly, a lot of times the dementia means that if somebody has arthritis or has pain, they cannot express it. If you ask the CMA that may not have been trained, or a nurse that hadn't been trained they're going to say this is a prn pain drug, he's not going to ask for it because he can't. So you have to look for other things. So one of the initiatives that CMS has right now going on, that nursing homes are getting cited for all over the country is identifying people with pain. The one that was just like this about five to seven years ago, was identifying people with depression. Well, we started our depression initiative seven years ago. We only had like 5% of the people because we just didn't know how they do that. Now we have 30% of the people usually being treated, but pointing to your question is when you're going for behavioral issues in long term care, you don't want to go to the antipsychotic unless you have to, because antipsychotics intuitively have more side effects than other things, so what we teach is you rule out pain first and a lot of times, I've given somebody a COX-2 inhibitor, you will get, that person's behavior will go away because the dementia, that causative factor went away. It's kind of like saying, you know if somebody has an appendicitis, you treat the appendix, you don't do something else. Then you, the next thing is you rule out depression, and that's why this is very much of interest to me. The next thing you do, is then you use a drug that you can utilize for behaviors with the least amount of side effects. And we used to use things like, a lot of people still use Lorazepam or Ativan, but Ativan has a high incidence of falls, fractures, disinhibition, which basically means it acts like alcohol. And a lot of people will take off their clothes, they'll act inappropriately. And we've been finding out that a lot of these seizure medications like Divalproex or Depakote work very well with minimal side effects, so we'll go there. In other words if you notice what I've talked about, we'll do everything we can to not go to an atypical, but if we have to, when we go to the atypical, we want to go to the atypical that has the most effect with the least amount of side effects.*

Dr. Graham: *Has your benzo use decreased?*

Dr. Mason: *Over time, yes.*

Dr. Graham: *Because we don't see that. We don't see that in the nursing home population. Matter of fact, we see more and more requests for benzos.*

Dr. Mason: *I can't, I cannot speak for the entire nursing home population because we have one segment of it, but I can say most physicians are still writing for Lorazepam. However, we are educating them on a day to day basis that that is not necessarily the best thing to do. It's just like, and the other part about this that I guess should be fair, is that when I was 18 years old, I was a nurse's aide in a nursing home and became a CMA, so I didn't know I would wind up here. I have worked community. I have worked hospital. I have taught at SWOSU school of pharmacy. But I've chosen this because I really do enjoy it and I feel like I can make a difference. But to get back to your questions, the benzos, until even three, four years ago, we thought that it was the way to do things. Time is changing and most people recognize it that the less benzos you use, the better off you are. However, you're still going to have to, the only, the only thing I'd like you to consider is that we call ourselves Senior Care pharmacists now, not long term care pharmacists, and the reason we do that is because even though traditionally we've learned our skills in long term care, 90% of the people are at home. My mother and father are at home. My in-laws are at home. And we're going to get enough work. There's going to be people that need to go to the nursing home. And what we're really about is educating people so that these people can continue to live a quality of life the best they can because most of the time when people come in, into the nursing home, we see the therapy they're getting in ambulatory care. It's not necessarily the choices that we would give geriatrics for good health.*

For Public Comment, David McElwain: *I do appreciate your giving me the time to speak. I'm a psychiatrist practicing in Tulsa and I've worked with various Medicaid populations for over twenty years. My main Medicaid population now is a group of mentally retarded adults. I treat about 300 mentally ill adults who used to be at Hissom. They're now living in the community in Tulsa. The biggest challenge with that population has been their tendency towards behavioral disturbances and aggression in the community, and to follow up on what you were just saying, much like the elderly, the demented population sometimes they're non-verbal and very aggressive, and the SSRIs has been a wonderful class of medication to control their aggression. And I've had a great success in tapering them off the traditional and the novel antipsychotics and getting them on an SSRI. In particular, Celexa and Paxil have been wonderful at calming aggression and sometimes getting people completely off antipsychotic agents. I think psychiatrists have always been cost-conscious. Most of us got our training in community mental health centers and had a limited formulary from the get-go. So we're very familiar with having a restricted formulary and trying to pick which one we could. Also following with what Dr. Ware said, for me, the two best indicators of what SSRI to pick for a particular patient are personal history, which ones they've tried, what experience they've had with which ones, and also family history. I don't think anyone's mentioned that yet. Tendencies to respond to SSRIs definitely run in families. If I meet a patient and they've got two sisters who've great on Zoloft, gosh, I'm looking at Zoloft. And if you really tie my hands and eliminate all those choices for me, it's going to make, it's going to make it much*

more difficult to get it right the first time. All the things the other two, the other two speakers have said are absolutely true. I agree with the need for less restriction. It's really going to make our jobs much more difficult. The other thing is, about cost. We are making a, the SSRIs do tend to cause weight gain. As a class, they tend to promote weight gain over time, some more than others. That is a particular problem with my population. Maybe not with your patients, but certainly my folks are obese. Many of my patients are overweight and tend to gain more and more weight. I have a lot of folks who are also on Depakote, also on antipsychotics and I'm always trying to find some combination to help minimize their weight gain. It certainly is my experience that Paxil CR does cause less weight gain and I have had patients who have lost a lot of weight since switching them from traditional Paxil over to the Paxil CR. So, in particular, I'm hoping that Paxil CR can be an option when ya'll make a decision. In particular when you're talking about costs and looking at the analogy of using the atypical antipsychotics. Because weight gain has been such a big problem with some of the antipsychotics, we've gotten, we psychiatrists, we've gotten in the habit of adding generic glucophage. For a lot of those patients, if you add glucophage, you can prevent hyperglycemia and tend to offset, we hope in the long run, offset their tendency to develop diabetes. There's some new evidence too, that low dose Depakote has some statin abilities, and maybe we'll offset some hypercholesterolemia. So if you're looking at costs and we're going to end up using only generic SSRIs, by the time we add Metformin and by the time we add Depakote or valproic acid to everybody, you're not going to save a lot on costs. And those are going to slide through prior auth. So not even thinking about the costs of hospitalization and the cost of EKGs and the extra visits to the doctor because of the obesity, I think you really need to look at the cost of just the pharmaceuticals. That's it. Questions?

Dr. McNeill moved to prior authorize SSRIs (with change to no. 2 of tier-2 recommendation to read, *"Failure with a tier one medication defined as no beneficial or minimally beneficial response after at least 4 weeks of continuous use."*; motion seconded by Dr. Swaim.

ACTION: MOTION CARRIED.

AGENDA ITEM No. 7: **DISCUSS & VOTE ON PRIOR AUTHORIZATION OF ARBs**

Materials included in agenda packet; presented by Drs. Moore and Gorman.

For Public Comment, Dr. David Browning: *I'm a practicing internist and nephrologist and I just noticed moments ago that Dr. Payton in this city and others spoke at last meeting in general about the angiotensin receptor blockers and in particular about Irbesartan/Avapro. So I've just thrown my little five minute outline out the window of my mind and I'm going to make a couple of comments. We need to do more about diabetes. It is in some senses, a national and Oklahoma threat to the health of our society; certainly to the individual. And it's also in some sense, something of a disgrace. Diabetes Type II is also in part, a disease of choice and a cultural disease, as you know. But we now are seeing children and adolescents with Type II diabetes and I called and got the end stage renal disease network data. Network 13. Maybe you know that the federal government sees to it that all of the end stage RD patients are enumerated and monitored for the four state area. In 2002, there were newly diagnosed ESRD patients in the number of a 1,017. In 2003 that number was 1,400. That's virtually a 50% increase, an asymptotic curve. And that's borne out nationally. Presently 410,000 patients in ESRD projected by 2010 to be 650,000. And it's not end stage renal disease on dialysis is not an easy life. One of the more dramatic things that I've seen in my time as a physician, years in service getting to be some number, is the development of angiotensin receptor blocker. ACE inhibitors were really good a generation ago and gave us capabilities that we did not have as clinicians, as internists or nephrologists or whatever. But the angiotensin receptor blockers which is a downstream effector as you know, at the cellular receptor, blocking angiotensin 2 activity and vasoconstricted effect on the angiotensin 1 receptor dramatic. And particularly, talking just about diabetics for a moment, there is now abundant evidence that ARBs and to some extent ACEs can halt or slow or even reverse the progression of diabetic nephropathy to end stage renal disease. It is dramatic, reductions in the amount of proteinuria which is our nephrologist index of how bad things are going, one index, serum creatinine being another. So it's a dramatic time. And I think it's only the beginning because it's not only in AT 1 receptors, and AT 2 receptors, vasodilator and goodness knows what sort of messenger pathways to the "illegible". There's a lot of interesting things coming down the pike, but the ARB era is here. I don't know and I'm not going to even comment on the economics. I realize the physician is over his head. Actually I sat on one side of this table a long, long time ago and I know something about limited resources or setting priorities. I'm not going to talk about economics. There are tools and mechanisms and I can even give any of you a reference for pharmacoeconomics, for example Irbesartan. Lives saved and dollars saved and so forth. But that's not my point. You can figure those things out very well. It is very, the ARBs are a very effective tool and I think they should be in what I understand to be Tier I which is a favorable position. I haven't been able to get a clear definition of Tier I and II, but I do know from my side of the desk as a practicing physician that stopping to write a letter or to go back and review the record for a failed, failed trial of another drug, all of that, it's an inhibition, and*

I think we ought to remove inhibitions for Type II diabetics in Oklahoma having access to ARBs, particularly if they have renal disease. If they do, JNC7 guidelines, the American Diabetes Association recommends clearly that ARBs be considered. We have two basic choices so far as the FDA is concerned. Irbesartan/Avapro and Losartan/Cozaar. I salute in my . . . because Cozaar was the first a generation ago, I salute it, but the truth is, in my opinion, Irbesartan/Avapro is a superior choice and it's what I use in my practice because it has more antihypertensive effect than Cozaar. Each has been shown in the RENAAL Irbesartan diabetic nephropathy trial to slow the progression of diabetic renal disease to end stage renal disease. You have a very nice tabulation of the pharmacology and pharmacokinetics of the ARBs someplace in your handout and I won't go through all that except to say that there a couple of things that I noticed that were missing as I scanned it. Number one, Irbesartan blocks the AT 1 cellular receptor 100%, the other ARBs do not. And that's really what we want to do, is block that bad molecule in angiotensin 2. Number two, Irbesartan has a dose response curve whereas probably Losartan has a much more "illegible" or nonexistent dose response curve, that is the more you give the more effect you get. Doubling the dose has an effect. And thirdly, angiotensin 2 inhibition continues longer with Irbesartan than with (TAPE END). *. . . evidence for renal disease would have tier 2 availability to ARBs. Thirdly I think we need, I hope we can find a way to promote and encourage the testing for microalbuminiuria. If we wait until the patient has 300 mg of protein a day in their urine, we're way down the road towards dialysis, and there's now abundant evidence of more coming. With the microalbuminiuria test picking up at 30, 40, 50 mg per 24 hours, then that Type II diabetic patient can really benefit from an ARB. You can slow that down, stop it, even reverse it. I mean it's, it's really dramatic. The microalbumin test isn't done very often in my experience. I talk around the state a bit and it's becoming more available. I don't know how laboratory testing is handled by the Authority, but I would certainly look at microalbumin testing as . . . the American Diabetes Association recommends that it be done at time of diagnosis of Type II diabetes and annually thereafter. In my hospital it costs unconscionably about $67.00, hospital lab, but I'm told at national meetings you ought to be able to get it for six or seven bucks. So, and then thirdly if it isn't being done, I would hope that there could be some kind of coordination of data that you all accumulate with what ESRD 13 . . . Network 13 people accumulate. They've got a pretty good database. So that you can see what happens to people over time. Are we having an effect on the deadly march of diabetes to end stage renal disease and death. And I would think that, that some interesting things could come out of that. I'd be happy to answer any questions.*

Dr. McNeill: *I have a question of the Board. The tiering of ARBs, are we talking about hypertension? Only hypertension?*

Dr. David Browning: *Well I was addressing . . . I was trying to narrow down my . . . Type II diabetes.*

Dr. McNeill: *I have a question for you in just a minute, please sir, but the Board . . . are we talking about just hypertension for the ARBs? Would type, would diabetic nephropathy, would that be a unique indication as the good physician has described?*

Dr. Nesser: *We could, we could make that . . .*

Dr. McNeill: *I mean, it's a standard of care . . . ACE inhibitors, ARBs, and to me that's a unique indication.*

Dr. David Browning: *I believe the FDA would agree with you. I believe that's standard position.*

Dr. McNeill: *Right. Thank you.*

For Public Comment, Dr. Chris Sholer: *Thank you very much for allowing me to speak. I addressed this group with a letter the last time. I wasn't able to make it, unfortunately, so I think this question came up several years ago in terms of the ARBs. I'm a practicing nephrologist here in Oklahoma City for about the past twenty years, and in fact, probably have been since my 30 years of doing medicine I remember studying with a physiologist who actually determined there were two beta receptors, so I've kind of grown up with this and certainly hypertension has been a big part of my practice and a big part of my interest. When we're treating 400,000 patients now on dialysis, and that's only the tip of the iceberg, that's going to double by 2010, the cost of that goes up. That's why these two studies were done. It all started in '93 with Captopril and I'm just going to briefly, just go this, in, with Type I diabetics only, showing that there was a definite improvement in renal protection, over and above blood pressure control. It was our first hint that it really made a difference how we treated these patients. Since then, there's not been a study done looking at outcome data until RENAAL and IDNT, and those were done in all Type II diabetics. Usually very significantly advanced renal failure. I mean, these people had creatinines of 3 on the average and most of these patients were, you know, predominantly GFRs in the 25 to 30 range. So we were already down on the curve. You're not going to stop these people from ending up on dialysis. All you're going to do is slow them down. We bought them, on the average, two years. Both studies. Excellent studies that were done. Same blood pressure control, everything. It all comes down to endothelial dysfunction. How do we reverse that? How do we stop the progression of endothelial proliferation in these patients? There is a difference between the ACE inhibitors and angiotensin receptor blockers in that regard. There is a difference in side effect profiles. There's a difference in how long these patients are going to take these medicines. And my concern is, is not only for the diabetic nephropathy patients, but the diabetic patient, and even the patient with significant essential hypertension. How are you going to control his blood pressure? How are you going to keep him on his medication? We all know that only 25% of*

patients who are being treated are adequately treated . . . or 25% patients who are hypertensive are being adequately treated . . . 50% of patients we're actively treating are at . . . are not at goal. You know. We're, we're not doing our job. One of the problems is it takes three to four medicines for most of these patients now to get under control. Monotherapy doesn't work. It's been shown over and over and over again. Backrus has data after data showing that the patients who got their renal function down to where you're only losing the 1% per year that we all lose as we age when we get to the age of 40 to 50, they had to be on 3.2 medicines and that was the average. We're seeing more and more combination data. ACE inhibitors and angiotensin receptor blockers. They're actually synergistic. If these drugs were the same, we wouldn't be seeing that. An angiotensin receptor blocker is not an ACE inhibitor without a clock. This is a whole different class of medications. Now I can't tell you which one is better. I know there are pharmaceutical companies that love for me to say that, but I can't. I can tell you there are three that have outcome data. Losartan, Irbesartan in terms of renal insufficiency. You know, and, and Diovan or Valsartan in terms of their heart outcome data and they also show significant decreases in proteinuria which indirectly will reduce kidney function, or indirectly reduce the kidney disease indications. You know, we're seeing a large number of these people with chronic kidney disease and it's my opinion that, and I tell family practice patients this, that if you don't have this patient on some type of angiotensin drug, and you haven't tried it, you could be, you know up for some real, some real problems. These, the angiotensin receptor blockers in, in study after study, show that about 85% are still on the medication two years down the line. ACE inhibitors is about 60 to 65%, and it goes down the line. You know. I would hate to see the whole caveat of angiotensin receptor blockers put on a tier 2. That would extremely hamper my practice. Dialysis patients, the ARBs are much better than the ACE inhibitors in terms of slowing, you know, and making their blood pressure a lot more evenly controlled. Of course, by then, they've lost the ball game. But now I'm treating heart disease. Now I'm treating congestive heart failure and we know that works in these patients. We know that ACE inhibitors have a different effect on the heart than they do, than the angiotensin receptor blockers. I mean, ACE inhibitors lower left ventricular and diastolic pressure, where the angiotensin receptor blockers effectively reduce left ventricular mass. And there's a difference. They work in different sites. And it may have to do that when you attack the AT-1 receptor, you actually still have angiotensin 2 floating around and it's, it brings forth somehow, we don't know how, it brings the AT-2 receptor now expresses itself. For some strange reason, the angiotensin 2 can now hook onto that and actually cause vasodilation. This is where we think it actually improves endothelial function. And there have been numerous animal studies and now some human studies showing that it actually improves endothelial function by itself, where the other classes do not. This is where it lies. This is where we have to attack this. Unfortunately, the, you know, 50 million patients with chronic kidney disease that I'm seeing, you know, I'm not seeing all of them actually, but you know, they're out there in the country, they're all going to die of heart disease before they get on dialysis. I mean, that's the reality. Most of them will end up dying of heart disease, stroke, whatever, before that. The morbidity and . . . of just taking care of these people in a nursing home with strokes and stuff. If we can just slow this down, it's going to effectively reduce our nursing home population, it's going to reduce hospitalization. I'm seeing that now in my practice. I can tell you I've got about 50 patients who I know would be on dialysis by now without these drugs. They're well tolerated and typically I'm using an ACE inhibitor and an ARB, especially early on. The earlier I can get them, the better. I made a bold statement about 10 years ago that I've had to retract. I got a group of family practice physicians in Ponca City and I said, you know, doing microalbumins is a waste of time. And they all, of course, just jumped on me like crazy. I said, no, I said . . . if you have a hypertensive diabetic, you're going to use an ACE inhibitor, right? Right. So why check it. You know. It's an expensive test. Well, now I've changed my mind. I've had to reverse that. My idea still holds. You have a hypertensive diabetic, you're going to choose an ACE inhibitor or an ARB, but you now have singled out that patient who is at high risk for having a coronary stroke, coronary heart attack, stroke, whatever. You're going to be much more aggressive in that patient. That patient now has to have a blood pressure of 125/75, not 140/90 . . . 140/90 isn't good enough. We know that. You know, their renal deterioration is four to five times what a patient with 125/75 is. You know, reducing the cost I understand. I'm hoping the cost of these comes . . . come down, even for my population, but it's my first line of choice. I know these patients stay on it. There's less hyperkalemia problems than with ACE inhibitors. You know, forgetting about the cough and the angioedema, we know that. You know, those patients obviously have to be on an ARB if you treat them with an ACE. But the data is more compelling now. There'll be more data in about two years on combination therapy and actually head-to-head ACE/ARB stuff, and I'd like for us to wait for that to come out before we just eliminate this whole class from a tier 1. That'll significantly hamper our practice and, I mean, I, the analogy to me would be well, let's just take off the hydropiridine calcium channel blockers because we have Verapamil, and we have Cardizem™. No, they're different drugs. I mean, it, it's apples and oranges here. They're both fruits, but one's an apple and one's an orange.

Dr. Gourley: *About your end stage renal disease patients, how many would you say are diabetic and how many not? Like, are we talking about 90% of the patients have diabetes . . .*

Dr. Sholer: *Oh, no, not that many. It's actually reaching in the about 65 to 70% range. When I started in 1982, with, 1980, with Jim Peterson at the University here, 20% were diabetics. He made a bold statement that 50% by the turn of the century would be diabetic and he was off. It's about 60%.*

Dr. Gourley: *So the increase has been not only in the diabetic population but in other populations, too.*

Dr. Sholer: *No, the other populations, actually hypertension has come down some because of our effective treatments. Lupus and other diseases are about the same, other glomerulernephritis. We haven't seen a rise in it. The rise in the onset of all the ESRD patients, if you look at the curves, it's all diabetes. You know. Diabetes is an epidemic, the way we eat, the way we don't exercise, all of that comes into play, you know. But, you know, the patients that we're seeing, they, they're getting older, we're keeping them alive longer. We're doing bypasses, we have better heart medication, so the patients that I normally wouldn't have seen ten to fifteen years ago because they would have died, I'm now seeing. I'm seeing 70 and 80 year old people, where their kidney functions are deteriorating. You know, once they get down to 10 to 15% they need dialysis, you know. And a lot of them are diabetic. And you know, twenty years ago, they wouldn't have made it, so . . . it's a catch-22.*

For Public Comment, Evie Knisely: *I am Evie Knisely and I am a regional account scientific associate director with the scientific operations division of Novartis. And I'd like to talk to you tonight about Diovan. And John is passing out a handout that you should have seen last month at your meeting, actually one of my colleagues put this handout together and presented an overview of all of the clinical trial data around Diovan. So I'm not going to cover that tonight, but there's a couple of things that I wanted to bring to your attention, and just to reiterate what's been said by some of the other speakers. The two points that I'd like to address are that the ARBs should be first line and secondly, if the ARBs are first line, or if you choose to use an ARB, that you would choose to use Diovan. And the argument I think that supports first line use of the ARBs has really already been presented by the last two speakers, and I believe that's JNC 7 and of course the ADA guidelines. The fact that we have been directed by good consensus guidelines to use ACEs and ARBs in compelling indications for hypertensive patients. Okay, so we've got either and ACE or an ARB, now how do we choose to use one or the other? And I think the argument for using an ARB over an ACE is based on the versatility and the persistence data that we have for Diovan and that we have for the ARBs as a class. If I could call your attention to the first bullet point on the handout, this is indicated for hypertension with 24-hour blood pressure control, there are several studies, actually eight studies listed for you that use comparators, they all start versus comparator, and the second study and the third study both used ACE inhibitors, Lisinopril and Allopril. And what they found in these studies is that Diovan is as effective in terms of hypertension control as the comparator, either as effective or better. But they also found that in every case, Diovan is better tolerated. And that's really in all of our studies across the board. Patients do better on ARBs versus ACEs. And if you'll look at the last bullet point, which is superior, tolerability and adherence, I wanted to point this study out to you. This is actually a study of a managed care population. This is a Merck Medco population and this particular work looked at persistency and they compared Diovan, a calcium channel blocker, Norvasc and then Lisinopril as the ACE inhibitor. And what they found is that persistency was superior for Diovan. They had 63% persistency versus 50% for Lisinopril and 53% for Norvasc. And that did achieve statistical significance. Patients were 1.5 times more likely to discontinue therapy if they were on the ACE inhibitor Lisinopril versus Valsartan or Diovan. So I think both of those arguments can support the use of an ARB first line. Now if you choose to use an ARB, we'd like you to choose Diovan. The reasons for that reallly are the entire worksheet that I've put in front of you, because our clinical program is very strong, very robust. Novartis as a company, has done a very good job of putting money where their mouth is, and doing good outcome trials with our products. And I think the best job has been done with Diovan. You can see the trials, we have good, good outcome trials with hypertension, we have good outcome trials with heart failure, and of course, post MI. We do currently have an indication for hypertension and for heart failure. We're hoping to get one for post MI. That's in the works with the FDA. So based on the superior clinical program we have, we have studies, we have the most patients in clinical studies of any ARB on the market. So based on that and based on the tolerability, I'd like you to consider ARBs first line, and then Diovan as your ARB of choice. Any questions?*

For Public Comment, Mat Kumar: *My name is Mat Kumar. I'm with AstraZeneca as a medical informational scientist. My background, I have a very good degree, but I spend most of my time in basic research. And sometimes in clinical trials, too. For all the clinical trials with which I was associated is with Candesartan that is marketed as Atacand. During that clinical trial I happened to hear from a patient and particularly from one patient who said that his blood pressure is well controlled and there are no side effects like headache, nausea, like ankles swelling, those kind of things. Our patient says that because he knew that, you know, some patients may be on placebo, so his blood pressure was controlled. This is a very experienced patient who knows that his blood pressure is well controlled, so he knows that he's on Atacand. And then there's no side effects. So that indicates, I think, needless to say, that the clinical trial was with Candesartan and like the patient said, that the blood pressure was well controlled. To reiterate that comment, the trough to peak ratio of Candesartan is over 80%. Now that's one of the highest in the ARB class and that's important because most of these incidents occur in the morning. At that time, the patient may*

not be taking that drug, so at that time the blood pressure control is critical. So here we have a situation where even 24 after the dose, the patient's blood pressure is controlled 80%. Now from "illegible" I'm going to focus on four key issues. One, of course, will be no side effects. Two, no interaction with cytochrome P450; and number three, of course, well controlled systolic and diastolic blood pressure with qd dosing. And finally, I'll focus on the heart failure study, it's called CHARM, where we looked at patients treated with ACE inhibitor . . . with ACE inhibitor plus, ACE inhibitor plus Candesartan . . . no ACE inhibitor plus Candesartan, and the patients who have diastolic dysfunction. So some of the trials I will focus are one is a claim which clearly indicated the superiority of Candesartan over Losartan, over 24 and 48 hour dosing period, and where it was clearly shown that the blood pressure is well controlled, is superior to Losartan. Second, there is another study by Morganson who indicated that the UCA, the urinary creatinine albumin ratio is reduced in Type II diabetes patients with hypertension when they are treated with Candesartan. And also, a study showed that there is a reduction in left ventricular mass in hypertensive patients treated with Candesartan over 24 weeks. Now that study has been confirmed in "illegible" both invitro and in vivo short reduction in rats in that particular mass. And finally, I will focus on CHARM clinical trial. This trial is done with heart failure patients, three arms; one without ACE inhibitor, one with ACE inhibitor, and the third one in diastolic dysfunctional patients. The patients without ACE inhibitor, the reduction in mortality and morbidity is over 12%. That's a significant number. And in patients who are treated with both ACE inhibitor and Candesartan the reduction in mortality is observed and there is a significant reduction in the morbidity than in of a hospitalization of the patients. And with the third arm, with the diastolic dysfunction. Tthis is the first time I proved a drug has been tested in patients with diastolic dysfunction and they have shown that there is a reduction in morbidity, even though it is not statistically significant, but still it gave an indication. So, overall CHARM clearly indicated that there is a reduction in mortality and morbidity in heart failure patients with Candesartan treated over 26 weeks. And I would like to spend a little bit time with binding, someone has mentioned. Candesartan also has 100% binding. In fact it has longest binding, and I think we should focus more on peak to trough ratio. That's one clearly indicates how effective the drug is in controlling the blood pressure. So with that I am open for questions.

The Board members asked Dr. Sholer and Dr. Kumar questions to clarify issues related to this agenda item.
Dr. McNeill moved to accept the recommendations and prior authorize ARBs with the addition of: *5. Clients with diabetes would be exempt from requirements of step-therapy*; motion seconded by Dr. Gourley.
ACTION: MOTION CARRIED.

AGENDA ITEM NO. 8: **DISCUSS & VOTE ON MAINTENANCE DRUG LIST**
Materials included in agenda packet; presented by Dr.Gorman.
Dr. Meece moved to approve the maintenance drug list as submitted; motion seconded by Dr. Swain.
ACTION: MOTION CARRIED.

AGENDA ITEM NO. 9: **REVIEW & DISCUSS ANTIBIOTIC UTILIZATION**
Materials included in agenda packet; presented by Drs. Le and Gorman.
For Public Comment, Dr. Jason Sigmon: *Thank you. I have to admit, after . . . as a practicing otolaryngologist, the last hour and a half has been a combination of a review of medical school and cold sweats thinking about serotonin reuptake inhibitors, ACE inhibitors. But I think that that was actually good for me. God works in wonderful ways and I think I was meant to be number nine at 7:55 in the evening. This isn't an action . . . an action on the agenda, it's a discussion on utilization review for antimicrobials and obviously will be prone to more specific discussion about antimicrobials as they are involved in utilization review. But I'm an otolaryngologist in private practice in Oklahoma City and my practice interests include the medical and surgical treatment of acute and chronic sinusitis. I want to discuss briefly, since this was on the agenda, some of the latest guidelines from the Sinus and Allergy Health Partnership. It was released in January of 2004 and this is a . . . the Sinus and Allergy Health Partnership is a multidisciplinary board that is made up of members of the academy . . . American Academy of Otolaryngology, head and neck surgery, of which I'm a member, as well as the American Academy of . . . the American Larynogologic Society. It also includes the American Academy of Otolaryngology, and what's interesting about the Sinus and Allergy Health Partnership as it involves antimicrobials is that this is a multidisciplinary board that is trying to look at outcomes as it regards upper aero digestive tract pathogens, specifically with the sinuses, obviously, but it's a group of specialists that is really involved almost for in acute exacerbation of chronic disease in the sinuses and also complicated sinus infections such as periorbital cellulitis and some of the things that are more urgent issues. But the published guidelines and the aims of the Sinus and Allergy Health Partnership was directed primarily at acute sinusitis and the impetus for those guidelines and the reason why they focused on acute sinusitis*

was because of the emerging national, regional resistant patterns for upper aero digestive tract pathogens, specifically strep/pneumo. And we're all familiar with and, this is kind of preaching to the choir, but with pharmacists here it makes me nervous, even, you know, mentioning anything as it regards to pharmacology and upper aero digestive tract disease. But in my clinical practice, the, the issues with antimicrobial resistance are, are real, and you know, ever present. And fortunately, these pathogens have not changed over the last four years, but the resistance obviously has. We're seeing alarming increases in, I mean, everyone is familiar with penicillin resistant strains. Meanwhile, we're also seeing an alarming increased resistance in macrolide resistant strep/pneumo and the Sinus and Allergy Health Partnership, their direction at presenting antibiotic guidelines for acute sinusitis is really, focuses on preventing continuation of this resistance pattern. Now what the Sinus and Allergy Health Partnership did was divide the acute sinusitis into mild disease, and mild disease and moderate disease. Now the mild disease is divided twice and the reason for that is that they felt necessary to divide the patients who have mild based on symptom score, or based on prior antibiotic usage versus no prior antibiotic usage. And so a patient who comes in with mild acute sinusitis based on symptoms who has no prior antibiotic usage has a different criteria for their guidelines for therapy; whereas those patients who have mild based on symptom score with that prior antibiotic usage trigger a whole other level of guideline recommendations for antimicrobials. Specifically in terms of their recommendations for mild with no prior antibiotic usage. They start with Augmentin and aminopenicillins, which is Amoxicillin and then later generation Cephlasporins. In those patients who have mild based symptom criteria but also have prior antibiotic usage which is pretty much makes up all of my clinical practice, they're recommending the high dose Augmentin versus newer generation a-methoxy fluoroquinolones such as Gatafloxacin and Amoxifloxacin. My point for discussing the guidelines within my specialty is to try and emphasize my hope that as the Health Care Authority and Board begins the review process, that that review focuses on not only the economics of these newer generation antimicrobials such as the a-methoxy and fluoroquinolones, but also on disease specific factors that are affecting the economics of that disease beyond just the . . . beyond just the simple treatment of acute sinusitis. And, and I think that these, the review of these health guidelines as they reflect each disease's spot, whether it's community acquired pneumonia, acute exacerbation of chronic COPD, uncomplicated skin and skin structure infections, looking at those specifically and then choosing antimicrobials based on those that have the broadest efficacy, and also have an impact on these emerging resistant patterns is going to be crucial for my clinical practice in the future. Thank you. Any questions?

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 10: **FDA & DEA UPDATES**

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

ACTION: NONE REQUIRED.

AGENDA ITEM No. 11: **FUTURE BUSINESS**

11A: Hepatitis C Agents Review
11B: Epogen™/Procrit™ Review
11C: Benzo/Ambien™ Follow-Up Review
11D: Narcotics Review
11E: Xopenex Follow-Up Review
11F: Vote on Fuzeon™ Prior Authorization

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

ACTION: NONE REQUIRED.

AGENDA ITEM No. 12: **ADJOURNMENT**

The meeting was declared adjourned.

The University of Oklahoma College of Pharmacy

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

Memorandum

Date: August 02, 2004

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

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

Subject: DUR Board Recommendations from Meeting of July 13, 2004.

Recommendation 1: Discuss and Vote on Prior Authorization of Synagis™.

Recommended Criteria for Prior Authorization of Synagis:

A. Client Selection. Client must be included in one of the following age groups at the beginning of the RSV season:*:

1) Infants and children less than 24 months old with Chronic Lung Disease (CLD) who have required medical treatment (O_2, bronchodilator, diuretic, or corticosteroid therapy) for CLD in the 6 months prior to RSV season.
2) Infants less than 12 months of age, born at 28 weeks gestation or earlier
3) Infants less than 6 months of age, born at 29-32 weeks gestation.
4) Infants, up to 6 months old at the start of RSV season, born at 32-36 weeks gestation, who have 2 or more of the following risk factors:
    a. Child care attendance
    b. School-aged siblings
    c. Exposure to environmental air pollutants (Tobacco smoke exposure can be controlled by the family, so is not a risk factor for Synagis prophylaxis)
    d. Congenital abnormalities of the airway
    e. Severe neuromuscular disease
5) Children up to 24 months old with hemodynamically significant cyanotic and acyanotic congenital heart disease.
6) Infants up to 12 months old with moderate to severe pulmonary hypertension, cyanotic heart disease, or those on medications to control congestive heart failure.

* Treatment should continue through the entire RSV season.

B. Length of treatment. Synagis will be approved for use only during RSV season, as determined by Oklahoma State Department of Health, which is generally October 1 through April 30.

C. Units authorized. The number of units authorized is to be calculated as the closest number of full vials necessary to provide the dose based on 15mg/kg per month.

D. Dose-pooling. To avoid unnecessary risk to the patient, multiple patients are not to be treated from a single vial. Failure to follow this recommendation will result in referral of the provider to the Quality Assurance Committee of the Oklahoma Health Care Authority.

MOTION CARRIED.

Recommendation 2: Discuss and Vote on Prior Authorization of "SSRIs".

The following tier-1 drug list is recommended as a clinically acceptable combination for use as initial therapy for the majority of clients. The College of Pharmacy recommends this list to the Drug Utilization Review board for approval and referral to the Oklahoma Healthcare Authority for supplemental rebate consideration and final approval by the OHCA Board of Directors.

1. Fluoxetine (generic only)
2. Fluvoxamine (generic only)
3. Paroxetine (generic only)

The current restrictions on fluoxetine will remain in effect regarding the use of the 10 & 20 mg tablets and 40 mg capsules. All brand name medications will be subject to Prior Authorization requirements beginning July 1, 2004 when a State MAC price is applied to that product.

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

1. Documented adverse effect, drug interaction, or contraindication to the tier-1 products.
2. Failure with a tier one medication defined as no beneficial or minimally beneficial response after at least 4 weeks of continuous use.
3. Unique indication not covered by a tier-1 product.
4. Clients who have been on a tier-2 product within the last 90 days would be allowed to continue current therapy without interruption.

Currently paroxetine requires a prior authorization for clients less than 18 years of age. The following paragraphs are excerpts from the FDA Public Health Advisory, March 22, 2004.

"Today the Food and Drug Administration (FDA) asked manufacturers of the following antidepressant drugs to include in their labeling a Warning statement that recommends close observation of adult and pediatric patients treated with these agents for worsening depression or the emergence of suicidality. The drugs that are the focus of this new Warning are: Prozac (fluoxetine); Zoloft (sertraline); Paxil (paroxetine); Luvox (fluvoxamine); Celexa (citalopram); Lexapro (escitalopram); Wellbutrin (bupropion); Effexor (venlafaxine); Serzone (nefazodone); and Remeron (mirtazapine).

Among antidepressants, only Prozac (fluoxetine) is approved for the treatment of pediatric major depressive disorder. Prozac (fluoxetine), Zoloft (sertraline), and Luvox (fluvoxamine) are approved for pediatric obsessive compulsive disorder. None of these drugs is approved as monotherapy for use in treating bipolar depression, either in adults or children."

The current recommendations include fluoxetine and fluvoxamine as tier one for all ages. Paroxetine would continue to require prior authorization for clients under 18 years of age. Any further recommendations from the DUR Board regarding this age group would also be incorporated.
MOTION CARRIED.

Recommendation 3: Discuss and Vote on Prior Authorization of "ARBs".

The College of Pharmacy recommends placing the ARBs into the current Antihypertensive Medications Product Based Prior Authorization Tier 2 category.

The following criteria are recommended for approval of a Tier 2 ARB:

1. Documented trial of a Tier 1 ACE Inhibitor.
2. Documented adverse effect or contraindication to a Tier 1 product.
3. A unique indication for the Tier 2 drug which the Tier 1 drugs lack.
4. Current users will be grandfathered unless there is a 90 day break in therapy.
5. Clients with diabetes would be exempt from requirements of step therapy.

MOTION CARRIED.

Recommendation 4: Discuss and Vote on Maintenance Drug List.

The Oklahoma Health Care Authority has selected drugs from certain disease states that are considered maintenance medications because they are taken on a regular schedule to treat chronic conditions. These products, or maintenance drugs, may be dispensed for up to 100 units.

Anticoagulation:
cilostazol
clopidogrel
pentoxifylline
ticlopidine
warfarin

Asthma:
albuterol
albuterol extended release
albuterol/ipratropium
beclomethasone
budesonide
flunisolide
fluticasone
ipratropium
triamcinolone
salmeterol

Diabetic:
acarbose
acetohexamide
chlorpropamide
glimepiride
glipizide
glyburide
insulin
metformin
metformin/glyburide
nateglinide
pioglitazone
repaglinide
rosiglitazone
tolbutamide

Hormone:
conjugated estrogens
estradiol
estropipate
medroxyprogesterone acetate
tamoxifen

Cardiovascular (include combination where appropriate)
acebutolol
amiloride
amiodarone
amlodipine
atenolol
atorvastatin
benazepril
betaxolol
bisoprolol
bumetanide
candesartan
captopril
carvedilol
chlorothiazide
chlorthalidone
clonidine
diltiazem
digoxin
disopyramide
doxazosin
enalapril
eprosartan
ethacrynic acid
felodipine
flecainide
fluvastatin
fosinopril
furosemide
guanadrel
guanethidine
guanfacine
hydralazine
hydrochlorothiazide
indapamide
irbesartan
isosorbide mononitrate
isosorbide dinitrate
isradipine
labetalol
lisinopril
losartan
lovastatin
methyldopa
metolazone
metoprolol
mexiletine
minoxidil
moexipril
moricizine
nadolol
nicardipine
nifedipine
nisoldipine
nitroglycerin (all oral forms)
olmesartan
perindopril
pravastatin
prazosin
procainamide
propranolol
quinapril
quinidine
ramipril
reserpine
rosuvastatin
simvastatin
sotalol
spironolactone
telmisartan
terazosin
timolol
torsemide
triamterene
trandolapril
valsartan
verapamil

Thyroid:
levothyroxine
liotrix
liothyronine
methimazole
propylthiouracil

Other:
allopurinol
carbamazepine
colchicine
isoniazid
phenobarbital
phenytoin
potassium
prednisone
prenatal vitamins
primidone
rifampin
valproic acid

A motion was made to accept the previous list of maintenance drugs.
MOTION CARRIED.

PSYCHIATRIC MEDICINE
Kenneth W. Foster M.D. P.C.
P.O. Box 1041 / 604 Dewey Avenue
Poteau, OK. 74953
Ph: (918) 647-8420 Fax: (918) 649-0824

June 2, 2004

Ron Graham, DPh
Clinical Assistant Professor, DUR/Operations Manager
Pharmacy Management Consultants
University of Oklahoma College of Pharmacy
ORI-W4403 1122 NE 13th St.
Oklahoma City, Oklahoma 73117

Dear Dr. Graham,

It has been brought to my attention that the DUR Board for Oklahoma Medicaid is considering restricting access to certain psychiatric medications for patients enrolled in the Medicaid program. As a psychiatrist treating a large number of Medicaid patients I feel that significantly limiting the choices of medications that are available to clinicians would be detrimental to patient health. In my practice most patients present with a wide array of comorbidities along with underlying depression. It is critical that these patients are stabilized on a medication and not switched. The antidepressant I tend to choose most often is Paxil CR because it has a wide range of indication to cover those comorbidities, and a favorable tolerability profile. Both of these attributes tend to lead to patient compliance and a favorable resolution of symptoms.

I urge you to consider these issues as they relate to my practice, as well as other rural medical practices, in making your decisions.

Very truly yours,

KW Foster, MD

Kenneth W. Foster, M.D.

KWFMD/lw

Children & Adolescent Medical Services, Inc.
Scott S. Cyrus, D.O., FACOP
8803 S. 101st East Ave., Suite #200 ☺ Tulsa, OK 74133

23

July 10, 2004

Lynn Mitchell, M.D., Medical Director
Oklahoma Health Care Authority
4545 North Lincoln
Oklahoma City, OK 73105

RE: OHCA possible restriction to Synagis® (palivizumab) criteria.

Dear. Dr. Mitchell:

Throughout the past 5 years, I have taken care of many special needs and premature children in the Northeastern part of the state and the use of Synagis® (palivizumab) has played an important role. As a Tulsa pediatrician, one that is on staff at five hospitals, accepts Medicaid patients and works closely with the OHCA, I'm writing to you today to urge you not to limit the use of Synagis® (palivizumab) as currently proposed by the Oklahoma Health Care Authority Drug Utilization Review Board.

The Breath Easy campaign helps prevent the effects of smoking in restaurants and I believe the effects of chronic smoking in the home should be apparent that it plays a significant role with respiratory issues in our children. Smoking should be recognized as a criterion for the special needs child and premature child even as early as 35 weeks. Synagis® (palivizumab) can be used as a tool to prevent hospitalization and RSV in homes where smoking occurs.

The issue of using Synagis® (palivizumab) for six injections verses five is also apparent. As we've seen for many years, the RSV season can begin early in the fall and remain late in the spring. It's impossible to predict what the season will do and I wish the OHCA DURB would adopt a policy of monitoring the RSV in the state. Please don't possibly condemn our children to RSV early or late in the season because of this limitation.

Thank you for your attention to this issue and thank you for your time to serve in such an important role as member of Oklahoma Health Care Authority Drug Utilization Review Board.

Sincerely,

Scott S. Cyrus, D.O., F.A.C.O.P.

Scott S. Cyrus, D.O., F.A.C.O.P.

c: Thomas L. Whitsett, M.D.
Nancy Nesser, D. Ph., J.D.

INGRID W. JACKSON, M.D.

MERIDIAN MEDICAL TOWER
13321 N. MERIDIAN STE 314
OKLAHOMA CITY, OKLAHOMA
73120
(405) 755-2721

Dug Utilization Review Board
4545 N. Lincoln, Suite 124
Oklahoma City, OK 73105

Dear Board Members,

In response to your intent to require a prior authorization for SSRI"s, I'd like to respectfully object and ask you to maintain open access for Medicaid patients and providers for the following reasons:

1. In my clinical experience, not all SSRI's are the same. They differ in their selectivity, potency, and metabolism.
   A. Fluoxetine has a higher incidence of anxiety and agitation.[1]
   B. Paroxetine tends to cause more weight gain, muscarinic side effects, and serotonin withdrawal syndrome.[2,3,4]
   C. Fluoxetine, fluvoxamine and paroxetine are the worst offenders for P4502D6 drug/drug interactions.[5]
   D. Generics can have as much as 20% variability and do not have the same indications as the parents compounds.[6]
2. The prior authorization process takes a minimum of 24 hours to obtain approval. Medicaid patients may not return to the pharmacy 24 to 48 hours later for their medication, which means patients will go untreated. This could allow for relapse and/or possible hospitalizations, which would add an increased financial burden to the Medicaid system.
3. Many patients are currently well controlled on their SSRI. Grandfathering patients in the past has had some significant obstacles. Medicaid patients tend to changeproviders and pharmacies often. When this occurs, Medicaid patients have been denied their grandfathered medication.

Based on the negative impact prior authorization of SSRI's would have on Medicaid patients, and the increased cost burden to overall Medicaid system, I implore you too continue open access for this class of medications.

Sincerely,

Ingrid Jackson, M.D.
iwj/lb

[1] Prozac PI
[2] Fava, *J Clin Psychiatry*. 2002; 61:11, 863-867
[3] Richelson, *Mayo Clin Proc*, Nov. 1994, Vol. 69
[4] Coupland, *J Clin Psychopharmacology*; Vol. 16/No 5, Oct.1996, 356-362
[5] Preskorn, *J Psychiatric Practice,* Vol. 9, No. 3, 228-236
[6] GenevaRX.com

Laureate
Psychiatric Clinic and Hospital

6655 South Yale Avenue
Tulsa, OK 74136-3329
918.481.4000
918.481.4063 fax

www.laureate.com

Saint Francis Health System
Founded by The William K. Warren Foundation

July 1, 2004

Oklahoma Health Care Authority
Drug Utilization Review Board
4545 N. Lincoln, Suite 124
Oklahoma City, Oklahoma 73105

Dear Members of the DUR Board:

I am writing this letter to express my support for an open formulary concerning antidepressant medications. I understand that the DUR Board is considering requiring prior authorization for non-generic medications. There are scientific reasons why this would likely lead to difficulty with therapeutic choices. The generic choices of Paroxetine, Fluoxetine, and Fluvoxamine are good medications although they are prominent 2D6 inhibitors. Fluvoxamine is a very potent C1a inhibitor. This leads to potential drug interactions with other psychotropic medications including tricyclics and atypical antipsychotics. For this reason they would not be considered as first line therapy in people with comorbid depression and psychosis.

Zoloft and Paxil have been the medications of choice to treat anxiety disorders and their clinical trials have demonstrated efficacy across the board for these anxiety disorders. It would be desirable to have an alternative to generics, such as Zoloft, which has robust anxiety disorder indications, when treating anxiety disorders.

The more intangible aspect of patient care is that although serotonin reuptake inhibitors will successfully treat roughly the same number of people out of 100 individuals, it is rarely the same individuals that respond. Quite frequently, people switch from one serotonin reuptake inhibitor to another. To add the obstacle of prior authorization is more likely to delay or impair their ability to receive treatment than it is to save money. Noncompliance is quite common while people are waiting for the required time periods to pass during failed first policies. Failure can lead to worsening of symptoms, hospitalization, or even worse.

Please consider keeping the formulary open for serotonin reuptake inhibitors. Thank you for your consideration.

Sincerely,

Jeff Mitchell, M.D.
Vice President, Medical Director

JM/sm

J. FIELDS, M.D.
E. FOX, M.D.
500 E. Robinson
Doctors Park Suite 2600
Norman, OK 73071
(405) 364-6432

July 2, 2004

Dr. Lynn Mitchell, M.D.
Medical Director
Oklahoma Medicaid Program
4545 N Lincoln
Oklahoma City, OK 73105

Dr. Mitchell,

The office of Drs. E.M. Fox & J.E. Fields, LLP respectfully requests that the Oklahoma DUR Board give consideration to the following suggestions concerning Synagis and those who should qualify for it.

Low birth weight (less than 2500g) should be a risk factor. It has been clinically proven to pose a severe risk.

Smoking within the home is also a problem in Oklahoma that should be included as a risk factor to protect babies. Parents most likely will not cease smoking in the home or car even when in the presence of a high risk baby.

Lastly, please consider the fact that the number of Synagis injections needs to vary depending on the length of the season in Oklahoma. Typically our season runs October through late April or early May. Synagis should be given during the entire season.

Thank you for your consideration.

Sincerely,

Eileen M Fox, MD and James E Fields, MD

NAGAMANOHAR JAVVAJI, M.D.
333 South 38th St. - Suite A
Muskogee, OK 74401
(918) 682-8631

June 30, 2004

Lynn Mitchell, M.D.
State Medical Director
Ok. Health Care Authority
4545 N. Lincoln St. #124
Oklahoma City, OK 73105-3240

Dear Lynn:

On behalf of the ARB class, I am writing to request that the ARB's remain in a Tier I position on the State Medicaid System. Medicaid patients should be provided with the same standard of care as non-Medicaid patients. This would prevent Tier II prior authorizations from requiring unnecessary paperwork.

Thank you for your consideration.

Sincerely,

Nagamanohar Javvaji, M.D.

St. Anthony Hospital
CENTER OF BEHAVIORAL MEDICINE

1000 North Lee Street
Post Office Box 205
Oklahoma City, Oklahoma 73101

(405) 272-6065

June 16, 2004

DUR Board

Dear Members of the DUR Board:

I am writing this letter to express my support for an open formulary concerning antidepressant medications. I understand that the DUR Board is considering requiring prior authorization for non-generic medications. There are scientific reasons why this would likely lead to difficulty with therapeutic choices. The generic choices of Paroxetine, Fluoxetine, and Fluvoxamine are good medications although they are prominent 2D6 inhibitors. This leads to potential drug interactions with other psychotropic medications including tricyclics and atypical antipsychotics. For this reason, they would not be considered as first line therapy in people with comorbid depression and psychosis.

Zoloft and Paxil have been the medications of choice to treat anxiety disorders and their clinical trials have demonstrated efficacy across the board for these anxiety disorders. Arguably, Paxil and Zoloft are significantly different with their profiles regarding weight gain, anticholinergic effects, and sedation. It would certainly be desirable to have an alternative to generics, such as Zoloft, which has robust anxiety disorder indications, when treating anxiety disorders.

The more intangible aspect of patient care is that although serotonin reuptake inhibitors will successfully treat roughly the same number of people out of 100 individuals, it is rarely the same individuals that respond. Quite frequently, people switch from one serotonin reuptake inhibitor to another. To add the obstacle of prior authorization is more likely to delay or impair their ability to receive treatment than it is to save money. Noncompliance is quite common while people are waiting for the required time periods to pass during failed first policies. Failure can lead to worsening of symptoms, hospitalization, or even worse.

Please consider keeping the formulary open for serotonin reuptake inhibitors. Thank you for your consideration.

Sincerely,

Don Chesler MD

Don Chesler, M.D. Chairman
Department of Psychiatry
St. Anthony Hospital

List of signatures is available upon request.

30

Oklahoma Allergy & Asthma Clinic
Founded 1925

(405) 235-0040

750 N.E. 13th
(2 Blocks East of Lincoln Blvd.)
Oklahoma City, Oklahoma

MERCY OFFICE:
The Plaza Physician Offices
4140 West Memorial Road, Suite 115
Oklahoma City, Oklahoma

SOUTH OFFICE:
Southwest Medical Tower
1044 S.W. 44th St., Suite 518
Oklahoma City, Oklahoma

NORMAN OFFICE:
Physicians and Surgeons Bldg.
950 North Porter, Suite 101
Norman, Oklahoma

EDMOND OFFICE:
Sycamore Square
120 North Bryant, Suite A4
Edmond, Oklahoma

MAILING ADDRESS:
Post Office Box 26827
Oklahoma City, Oklahoma 73126

SPECIALIZING IN THE EVALUATION AND MANAGEMENT OF ALLERGIES AND ASTHMA IN ADULTS AND CHILDREN

Charles D. Haunschild, MD*°
James H. Wells, MD*+
John R. Bozalis, MD*+
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James R. Claflin, MD*°
Patricia I. Overhulser, MD*°
Dean A. Atkinson, MD*+
Richard T. Hatch, MD*°
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* Diplomate American Board Allergy and Immunology
+ Diplomate American Board Internal Medicine
° Diplomate American Board Pediatrics

G. Keith Montgomery, MHA
Chief Operating Officer

Ruth Riddles, BSN MBA CCRC
Clinical Research

Sherry K. Hubbard, RD LD
Clinical Dietitian

Karen Gregory, MS RN RRT AE-C CNS
Pulmonary Disease Management

Member Institution of
OKLAHOMA Health Center

July 26, 2004

Dr. Whitsett, DUR Chairman
4545 N. Lincoln Blvd; Ste 124
Oklahoma City, OK 73105

Dear Dr. Whitsett:

I am writing to request continued support of **XOPENEX** on the Medicaid formulary for children with asthma.

I have found this medication to be very effective and generally well tolerated in the young asthmatic. I have found nebulized **PULMICORT** and **XOPENEX** to be very, very helpful in the management of pediatric asthma.

Thank you for your consideration and assistance in this matter.

Most Sincerely,

C D Haunschild, M.D.

Charles D. Haunschild, M.D.
Diplomate, American Board
Allergy and Immunology

CDH:kp

Copy: Nancy Nesser, R.PH
Lynn Mitchell, Medical Director
Ron Graham

DAVID WHATLEY, M.D.

Pediatric & Adolescent Clinic
601 S.E. Washington
Idabel, Oklahoma 74745

Telephone (580) 286-4355
Fax (580) 286-4358

8/13/04

Dr. Whittsett DurChairman
Lynn Mitchell - Med Dir.
4545 N Lincoln Blvd #124
Oklahoma City, OK 73105

Dear Sirs:

It has recently come to my attention that Xopenex is coming up for Review by the DUR Board - I prescribe Xopenex because it doesn't cause my patients heart rate to become elevated - my pediatric patients respond much better to Xopenex than albuterol. The efficacy of Xopenex is superior to albuterol and I need this drug to be available to my patients since the majority of my patients are Medicaid recipients. Thank you for your consideration.

Sincerely,

D. Whatley

TriCity Family Clinic

300 NW 32nd
Newcastle, OK 73065
Phone: (405) 387-4546
Fax: (405) 387-4551

8/5/04

To whom it may Concern:

This letter is in reference to the product Xopenex available in doses of 0.63mg, 1.25mg. for use of treatment of Asthma, and respiratory disease associated with Broncho-spasms, chronic cough and COPD. I Strongly endorse this product and have much experience with treatment of my patients in our Family medicine Clinic.

I understand that you are Reviewing for use or addition to your Formulary. I would like to see this medicine available for all my patient who experience chronic or acute asthma or COPD with Bronchospasm. I especially endorse the low incidence of tremor, insomnia, and tolerability of the nebulized use of Xopenex. Also less frequent dosing because of better Kinetics of the isomer-specific nature of Xopenex. Thank you for your Choice in Favor of adding

GERIATRIC MEDICAL SERVICES
Geriatrics • Longterm Care

June 30th, 2004

DUR Board

Dear Members of the DUR Board:

This letter is to express my support for an open formulary with regards to antidepressant medications. It has come to my attention that the DUR Board is reviewing the possibility of going to a prior authorization system for non-generic medications, with Fluoxetine, Fluvoxamine, and Paroxetine as the tier-1 products.

As a physician whose practice is dedicated solely to the geriatric population, the above referenced tier-1 products are never a consideration as "first-line" choices for the elderly. This is not because they are bad medicines; but from an evidence based medicine standpoint, it is well known that the above choices are prominent 2D6 and / or 3A4 inhibitors. Because of the high incidence of comorbid conditions in the elderly and the number of medicines they are taking for these conditions, it is in the patient's best interest not to prescribe prominent 2D6 and / or 3A4 inhibitors. Inhibition of medicines can result in increased side effects, falls, or even worse, dangerously low blood pressure levels.

Additonally, the above tier-1 products can have anticholinergic effects, which is always a concern in elderly patients.

Again, please consider the above reasons why the formulary for antidepressant medications should be left open.

Sincerely,

Kerry Cranmer, M.D., C.M.D.
Geriatric Medical Services

3545 N.W. 58th, STE 750, Oklahoma City

SHAWNEE MEDICAL CENTER CLINIC
SMCC

July 8, 2004

Oklahoma DUR Board
Oklahoma Medicaid Program
4545 N. Lincoln
OKC, OK 73105

TO: Whom It May Concern

RE: Synagis

It was brought to my attention that there are going to be some changes on the way for guidelines regarding the approval for Synagis use in premature babies. I would like to take this opportunity to voice my opinion. I understand that any child is prone to RSV, but the children who are born early miss out on the additional immune system to fight any kind of ear infections. This is worse for babies who have respiratory distress problem. Recently the Holman Paper has new date which clearly indicates that low birth weight babies are at a higher risk at contracting RSV during the epidemic period than non-low birth weight babies. Therefore, the weight and gestational age of the infant is an important factor when considering Synagis use.

I have noticed babies who wheeze and have tested positive for RSV around the year. Of course, the prevalence gets worse during the fall and goes as late as April. Therefore, cutting the number of doses down to five, as I am told, will not be beneficial.

I am a strong advocate against smoking. We all know, including all the parents, that smoking is an irritant to the respiratory system. Incidentally, the children, especially the newborns, have no say who smoke and where they smoke. They are left at the mercy of their caregivers. Smoking in the household is a huge contributing factor to the upper respiratory and lower respiratory illnesses. First of all, only half of the parents whose children were hospitalized accepted smoking cessation program. Of these, only half even try to quit smoking for more than 24 hours. Despite the fact that the parents are "educated" after the harm done to the babies, it is known that most caregivers continue to smoke at home. In my practice the older children have come and told me that their family still smokes in the house. Tobacco cessation programs unfortunately have failed to curtail smoking during and after pregnancy.

2801 N. Saratoga • P.O. Box 849 • Shawnee, OK 74802-0849 • (405) 273-5801 • FAX (405) 273-2632

I would therefore urge you to consider the tobacco smoke as an important and valid risk factor. Also the Synagis is recommended according to the AAP guidelines throughout the RSV season, which runs October through late April or early May in Oklahoma.

If you have further questions or concerns, please do not hesitate to contact me.

Kanwal K. Obhrai, M.D.
KKO:dlh
CC: Nancy Nesser, D.Ph, J.D.
Lynn Mitchell, M.D.
Thomas Whitsett, M.D.
Paula Root, M.D.

INTEGRIS
Family Care
Yukon

1205 Health Center Parkway
Suite 100
Yukon, OK 73099
(405) 717-5400

Family Medicine
Athena Friese, M.D.
Krista Schwarz, M.D.
Tanya Livingston, M.D.
Robert Lockwood, M.D.
Jeffrey M. Shadle, M.D.
Kimberly Kreymborg, PA-C

Pediatrics
Martha Arambula, M.D.
Dina Bowen, M.D.
Emily Reed, M.D.

June 29, 2004

RE: SYNAGIS DECISION

To Whom It May Concern:

It has been brought to my attention that the Board has decided to deviate from guidelines for Synagis. I would like to let the Board know that I feel as though it is important to consider environmental tobacco and smoke exposure when coming up with the guidelines. Children who are exposed to environmental smoke are at increased risk for severe respiratory disease and frequently parents are unable to stop smoking. Even if they are smoking outside these children continue to be at risk and I feel as though Synagis is appropriate for these children. I also am concerned about low birth weight children as low birth weight children definitely have increased risk with RSV exposure and I would like to prevent hospitalizations by providing them with Synagis. There is good data and literature within the medial community to substantiate this and has been the guideline and practice for many pediatricians. I would also ask that you reconsider the length of the RSV season here in Oklahoma. Our typical season will run from October and sometimes through May. We do have good virology reports through Children's Hospital and would ask that just five doses not be the current recommendation as it would be ashamed to cover a child for five months, just to have them hospitalized in April or May with RSV disease. I would ask that you reevaluate your current recommendations and follow the AAP guidelines, as this is what most pediatricians use and feel most comfortable advising our families through.

Sincerely yours,

Dina Bowen MD

Dina Bowen, M.D., FAAP
DB:slb

Richard A. Carlson, M.D.
Pediatrics

August 17, 2004

To Whom It May Concern:

I am writing to request that you continue to keep Xopenex on your formulary for asthmatic patients. I believe it is superior to Albuterol for a number of reasons. Chief among these are lower doses needed to affect bronchodilation and significantly lower incidence of side effects. I have a number of patients who have been on both medications, over time, and find that they respond better, faster and for a longer period of time on Xopenex vs. Albuterol.

Thank you for your consideration.

Richard A. Carlson, M.D.
RAC/aap

500 E. Robinson Suite 2200
Norman, Oklahoma 73071 (405) 364-7725

Respiratory Specialists, Inc.
1265 S. Utica, Suite 102 Tulsa, Oklahoma 74104 918/582-7007

Fred Garfinkel, M.D., F.C.C.P
Andrew Gottehrer, M.D., F.C.C.P.
Richard C. Beckendorf, M.D., F.C.C.P.

August 26, 2004

Oklahoma State Healthcare Authority
ATTN: Nancy Nesser, Director of Pharmacy Services
4545 N. Lincoln Blvd., Ste. 124
Oklahoma City, Ok 73105

Dear Ms. Nesser,

I am sending this letter asking that you seriously consider covering Xopenex (Single Isomer, Levalbuterol) nebulizer solution for Medicaid patients. I am a pulmonary physician who is director of pulmonary services and critical care at Hillcrest Medical Center in Tulsa, Oklahoma. In August of 2002 because of my knowledge of the harmful effects of the s Isomer of Albuterol, as well as my anecdotal experience of racemic Albuterol not getting the benefit that I desired, I chose to try using almost exclusively Levalbuterol in the hospital setting.

In the hospital we have kept accurate data on the effect of changing to predominantly Levalbuterol from racemic Albuterol. In evaluating 16 consecutive months of data, we were able to decrease our number of in hospital treatments by approximately 20%. We have decreased our number of missed treatments by approximately 30%. I believe these results are a result of the better therapeutic efficacy of the drug because of eliminating harmful effects of the s Isomer. Therefore we are able to achieve better outcomes with fewer treatments.

Based on the preceding information, I urge you to cover Levalbuterol (Xopenex) for all Medicaid patients. In my opinion, this will not only improve care of these patients, but overall will reduce their cost of care. I believe this is critically important to the Medicaid program. Although the drug acquisition cost may be slightly more, I anticipate based on my in hospital as well as outpatient experience that the patients will have markedly fewer episodes of decompensations and markedly fewer visits to an emergency room. Therefore, over all, their cost of care will decrease.

Thank you very much for giving this letter your consideration. I believe that doing this is in both the patient's and the state's best interest.

Sincerely,

F. Garfinkel

Fred Garfinkel, M.D.

APPENDIX B

Pharmacotherapy Management Program – Quarterly Report January - June 2004

Oklahoma Medicaid
September 2004

Summary of Program

Starting January 1, 2004, Pharmacy Management Consultants, at the request of OHCA, implemented the Pharmacotherapy Management Program. The mission of the program is to assist health care providers optimize safe and effective pharmacotherapy for Medicaid clients by minimizing adverse drug events and improving clinical outcomes. Currently, the Pharmacotherapy Management Program is only accepting Waiver clients. Clients may be referred into the program by physicians, pharmacists, or case managers. Waiver clients that require more than 3 brand prescriptions per month or 13 total prescriptions a month are automatically placed into the program.

After referral and receipt of necessary client information, the client's current pharmacotherapy profile is reviewed to identify drug-drug and drug-disease interactions, over and underutilization, unnecessary duplications, and potential opportunities to maximize the client's therapy and pharmacy benefit. Authorization requests are approved when appropriate and if the client meets PA criteria, if applicable. Physicians will receive correspondence outlining the program, its mission, and suggested changes to optimize the client's pharmacotherapy outcomes. The client's therapy will be reviewed again in several months to note any medication changes and suggest any further therapy modifications to enhance outcomes.

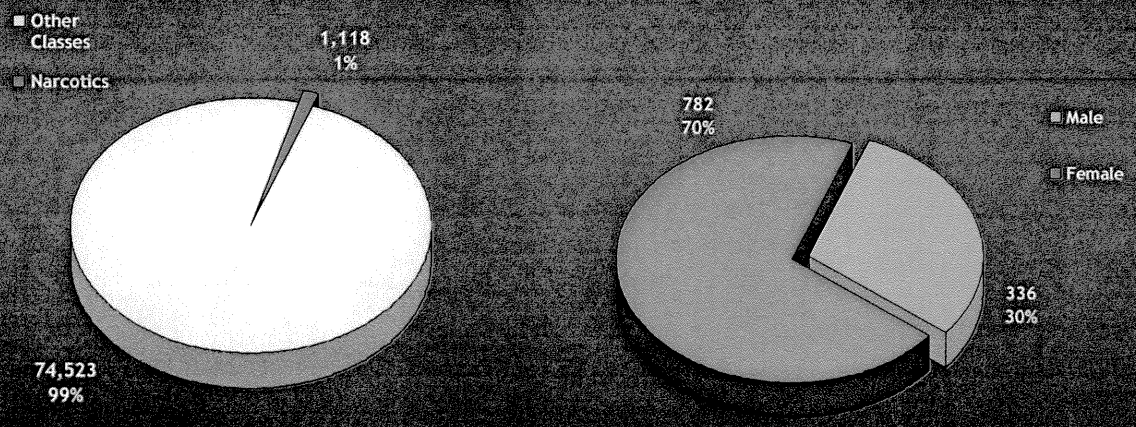
Pharmacotherapy Management Program Activity for January - June 2004

	Client Profiles Reviewed			Prior Authorizations				Communications	
Month	**# New**	**# Established**	**# Incomplete**	**Total**	**Approved**	**Denied**	**Incomplete**	**Letters**	**Calls**
Jan – May '04	564	0	n/a	2,930	1,535	195	1,200	n/a[1]	n/a[1]
June 2004	64	1	21	462	270	17	175	254	n/a[1]
Totals	**628**	**1**	**21**	**3,392**	**1,805**	**212**	**1,375**	**254**	**n/a [1,2]**

[1]Due to staffing considerations, certain productivity numbers were not logged during this time. Tracking mechanisms have been put in place to report these statistics.

[2]Call tracking started 7/19/04.

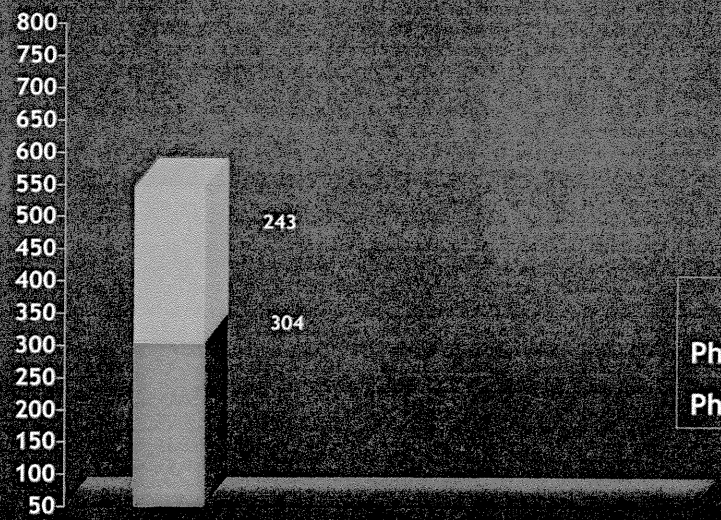
Oklahoma Medicaid RetroDUR Activity Report - Reviewed
May 2004 Narcotics - Females



PHARMACY Management Consultants

Oklahoma Medicaid RetroDUR Activity Report Follow Up
May 2004 Narcotics-Females 30-40 years

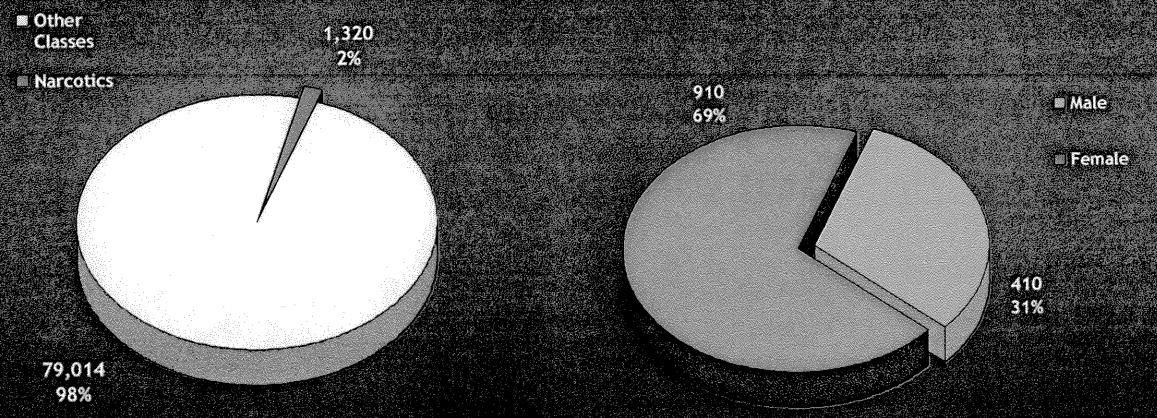
Total Reviewed = 547



Total Responses			
Pharmacy	=	235/335	70%
Physician	=	243/399	61%

PHARMACY Management Consultants

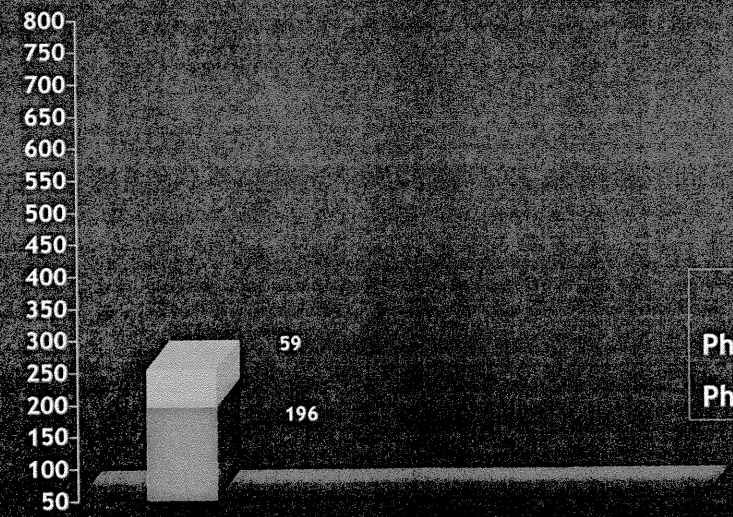
Oklahoma Medicaid RetroDUR Activity Report - Reviewed
June 2004 Narcotics - Males



PHARMACY Management Consultants

Oklahoma Medicaid RetroDUR Activity Report Follow Up
June 2004 Narcotics-Males 30-40 years

Total Reviewed = 255



Total Responses		
Pharmacy =	66/93	71%
Physician =	45/121	37%

PHARMACY Management Consultants

Michael Fogerty
Chief Executive Officer

Brad Henry
Govenor

STATE OF OKLAHOMA

OKLAHOMA HEALTH CARE AUTHORITY

Pharmacy Management Consultants
University of Oklahoma HSC
1122 NE 13th ST ORI-W4403
Oklahoma City, OK 73117

September 08, 2004

Dear

To assist the Oklahoma Health Care Authority in complying with OBRA '90 legislation, Pharmacy Management Consultants has implemented the Drug Utilization Review (DUR) Program to review client medication usage. The Oklahoma Health Care Authority continues to support the activities of the DUR program and its goal to ensure quality patient care for Medicaid clients.

The efforts of the DUR Program are intended to identify patients whose medication use may warrant review. Patient medication history profiles are confidentially reviewed for possible significance and, when appropriate, this information is shared with the patient's physician and/or pharmacist.

During review of the enclosed medication history profile, it was noted that your patient, may have the following

1) Use of Hydrocodone-Acetaminophen Oral Tab 7.5-500 MG and Hydrocodone-Acetaminophen Oral Tab 10-500 M represent a duplication in therapy based on their association to the therapeutic drug class NARCOTICS.

The DUR Board routinely notifies practitioners in these instances to ensure that this continued drug therapy is intended. This information is provided for you to review to ensure that this medication therapy is to be continued. Please remember that the findings of the review are based upon the information available at the time of review.

The DUR program is interested in learning of any measures taken in response to this information and/or comments regarding the current medication therapy. Please note your comments on the attached provider response form and return that form in the enclosed envelope. The patient profile and this cover letter are for your records and do not need to be returned. Thank you for your time and assistance in this review process.

Respectfully,

Ann McIlvain, PharmD
Clinical Pharmacist
(405) 271-6349
(800) 831-8921
Fax (405) 271-2615

Oklahoma Health Care Authority
Drug Utilization Review Program
Provider Response Form

Provider Id:

Prescriber Id:

Patient Id:

Screening Date: 05/01/04 through 05/31/04

This information is communicated strictly in confidence to the provider for evaluation and response:

- ☐ Record error. Not my patient.
- ☐ No longer my patient.
- ☐ Medication has been changed prior to date of review letter.
- ☐ I was unaware of this situation and will consider making appropriate changes in therapy.
- ☐ I am aware of this situation and will plan to continue monitoring this therapy.
- ☐ Other, comments.

Name (please print)

Signature

Please Return This Page Only

Pharmacy Management Consultants - PO Box 26901, Oklahoma City, OK 73190
Fax (405) 271-2615

PatientProfile:

Patient Id: Date of Birth:

Provider:

48

Total Distinct Medications: 16
Total Distinct Pharmacies: 15
Total Distinct Prescribers: 17

Date	Drug	Quantity	Supply Days	Pharmacy Id	Physician	Prescription Number
08/04/04	HYDROCO/APAP TAB 7.5-500	60	20			
08/04/04	NAPROXEN SOD TAB 550MG	60	30			
07/14/04	HYDROCO/APAP TAB 10-500MC	30	10			
06/30/04	PROPO-N/APAP TAB 100-650	60	7			
06/25/04	PROPO-N/APAP TAB 100-650	60	7			
06/14/04	HYDROCO/APAP TAB 7.5-500	24	3			
06/14/04	LEXAPRO TAB 10MG	20	20			
06/12/04	HYDROCO/APAP TAB 10-500MC	60	20			
06/11/04	TRAMADOL HCL TAB 50MG	30	7			
05/17/04	HYDROCO/APAP TAB 10-500MC	20	3			
05/14/04	HYDROCO/APAP TAB 7.5-500	20	5			
05/11/04	HYDROCO/APAP TAB 10-500MC	20	3			
05/07/04	CYCLOBENZAPR TAB 10MG	15	30			
05/07/04	HYDROCO/APAP TAB 7.5-500	30	5			
05/05/04	HYDROCO/APAP TAB 10-500MC	20	3			
03/12/04	HYDROCO/APAP TAB 7.5-500	50	4			
03/11/04	CEPHALEXIN CAP 250MG	40	10			
03/07/04	HYDROCO/APAP TAB 7.5-500	50	4			
03/05/04	HYDROCO/APAP TAB 10-500MC	30	5			
02/24/04	PROPO-N/APAP TAB 100-650	120	30			
02/22/04	HYDROCO/APAP TAB 7.5-500	30	2			
02/16/04	HYDROCO/APAP TAB 10-500MC	30	5			
02/15/04	HYDROCO/APAP TAB 7.5-500	30	2			
02/13/04	HYDROCO/APAP TAB 10-650MC	40	6			
02/11/04	HYDROCO/APAP TAB 5-500MG	20	7			
02/08/04	HYDROCO/APAP TAB 10-650MC	40	6			
01/28/04	HYDROCO/APAP TAB 10-500MC	30	5			

Date	Drug	Quantity	Supply Days	Pharmacy Id	Physician	Prescription Number
01/23/04	PROPO-N/APAP TAB 100-650	120	30			
01/19/04	TRAMADOL HCL TAB 50MG	60	7			
01/15/04	HYDROCO/APAP TAB 10-500MC	30	5			
01/13/04	DOXYCYCL HYC TAB 100MG	20	10			
01/13/04	TRAMADOL HCL TAB 50MG	60	7			
01/12/04	HYDROCO/APAP TAB 7.5-500	30	2			
12/03/03	PROPO-N/APAP TAB 100-650	120	30			
11/04/03	CEPHALEXIN CAP 500MG	40	10			
11/04/03	PROPO-N/APAP TAB 100-650	120	30			
11/04/03	ZOLOFT TAB 100MG	100	100			
10/15/03	HYDROCO/APAP TAB 10-500MC	25	3			
09/11/03	HYDROCO/APAP TAB 5-500MG	20	5			
09/05/03	NAPROXEN TAB 500MG	100	50			
09/05/03	PROPO-N/APAP TAB 100-650	120	30			
08/28/03	DARVON-N TAB 100MG	90	30			
08/27/03	CEPHALEXIN CAP 500MG	30	10			
08/01/03	PROPO-N/APAP TAB 100-650	120	30			
07/31/03	DARVON-N TAB 100MG	90	30			
07/03/03	PROPO-N/APAP TAB 100-650	120	30			
07/01/03	DARVON-N TAB 100MG	90	30			
06/10/03	CEPHALEXIN CAP 500MG	28	7			
06/05/03	CEPHALEXIN CAP 500MG	30	10			
06/02/03	PROPO-N/APAP TAB 100-650	120	30			
05/28/03	TRAMADOL HCL TAB 50MG	30	7			
05/01/03	TRAMADOL HCL TAB 50MG	30	7			
04/21/03	PROPO-N/APAP TAB 100-650	100	30			
04/07/03	HYDROCO/APAP TAB 5-500MG	10	3			
04/07/03	TRIMOX CAP 500MG	30	30			
04/03/03	PROPO-N/APAP TAB 100-650	60	15			
03/12/03	CEPHALEXIN CAP 500MG	40	10			
03/12/03	PROPO-N/APAP TAB 100-650	20	1			

Date	*Drug*	*Quantity*	*Supply Days*	*Pharmacy Id*	*Physician*	*Prescription Number*
03/04/03	PROPO-N/APAP TAB 100-650	120	30	[illegible]	[illegible]	
02/03/03	PROPO-N/APAP TAB 100-650	120	30			
01/21/03	CEPHALEXIN CAP 500MG	40	10			

(please keep this patient profile for your records)

Oklahoma Health Care Authority
Drug Utilization Review Program
Provider Response Form

Provider Id:

Patient Id:

Screening Date: 05/01/04 through 05/31/04

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- ☒ I am aware of this situation and will plan to continue monitoring this therapy.
- ☐ Other, comments.

Was Not Aware of all other Pharmacies & Physicians — will watch more closely —

Name (please print)

Signature

Please Return This Page Only

Pharmacy Management Consultants - PO Box 26901, Oklahoma City, OK 73190
Fax (405) 271-2615

Faxed 7-30-4

Oklahoma Health Care Authority
Drug Utilization Review Program
Provider Response Form

52

Provider Id:

Prescriber Id:

Patient Id:

Screening Date: 05/01/04 through 05/31/04

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- ☐ Other, comments.

Pt. was referred to a specialist - She cancelled or missed these appointments - requesting pain medication & excuses on not being able to make visits. Dr finally had to terminate Dr/Pt relationship due to non-compliance.

Name (please print)

Signature

Please Return This Page Only

Pharmacy Management Consultants - PO Box 26901, Oklahoma City, OK 73190
Fax (405) 271-2615

Oklahoma Health Care Authority
Drug Utilization Review Program
Provider Response Form

Provider Id:

Prescriber Id:

Patient Id:

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- ☐ I am aware of this situation and will plan to continue monitoring this therapy.
- ☐ Other, comments.

I have sent a dismissal letter to this patient. I suspected possible Abuse but until now it was not proven.

Name (please print)

Signature

Please Return This Page Only

Pharmacy Management Consultants - PO Box 26901, Oklahoma City, OK 73190
Fax (405) 271-2615

Oklahoma Health Care Authority
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Provider Response Form

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- ☐ I am aware of this situation and will plan to continue monitoring this therapy.
- ☒ Other, comments.

I called the other pharmacies to see if she was on file at the area pharmacies. She was last at ON 5-17-04

Thank you!

Name (please print)

Signature

Please Return This Page Only

Pharmacy Management Consultants - PO Box 26901, Oklahoma City, OK 73190
Fax (405) 271-2615

Oklahoma Health Care Authority
Drug Utilization Review Program
Provider Response Form

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Patient Id:

Screening Date: 05/01/04 through 05/31/04

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Name (please print)

Signature

Please Return This Page Only

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Fax (405) 271-2615

Activity Audit for

July 01 2004 Through July 31 2004

Date	Antiulcers app.	Antiulcers den.	Anxiolytic/ Hypnotics app.	Anxiolytic/ Hypnotics den.	Antihistamine app.	Antihistamine den.	Growth Hormones app.	Growth Hormones den.	Stimulant app.	Stimulant den.	Smoking Cess. app.	Smoking Cess. den.	Nsaids app.	Nsaids den.	ACE Inhibitors app.	ACE Inhibitors den.	HTN Combos app.	HTN Combos den.	Calcium Channel Blockers app.	Calcium Channel Blockers den.	Plavix app.	Plavix den.	NPA app.	NPA den.	Misc app.	Misc den.	Daily Total
1	78	29	248	37	31	18	4	0	33	20	0	0	18	24	5	4	1	2	5	9	27	4	19	6	0	1	623
2	57	36	248	40	22	20	2	0	47	11	0	0	16	36	4	5	2	1	6	15	28	5	14	10	0	1	626
3	7	6	47	3	8	1	0	0	13	5	0	0	1	8	0	1	1	0	2	1	3	1	1	5	0	0	114
4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6	21	23	221	30	43	23	0	0	44	28	0	0	7	27	6	6	3	3	3	17	43	3	12	6	0	0	569
7	30	33	269	38	47	22	0	0	69	26	0	0	13	31	3	7	1	1	6	16	46	9	8	4	0	1	680
8	15	38	193	33	30	36	3	0	63	15	0	0	10	24	3	5	1	4	6	7	32	9	19	12	0	1	559
9	15	22	171	21	37	26	0	0	66	21	0	0	15	19	2	4	1	2	7	17	36	3	21	8	1	1	516
10	3	1	46	11	11	7	0	0	11	8	0	0	3	4	3	0	1	0	4	2	8	0	2	0	0	0	125
11	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12	15	8	190	29	20	25	0	0	51	19	0	0	10	12	3	3	1	0	1	11	28	6	12	10	0	1	455
13	10	16	181	36	33	22	0	0	53	11	0	0	13	19	2	2	3	3	3	10	18	9	9	11	0	1	465
14	15	38	183	35	19	32	0	0	56	17	0	0	19	24	4	14	0	4	10	21	22	8	19	12	0	2	554
15	9	12	142	25	28	20	3	0	39	31	0	0	3	26	3	8	2	3	4	16	27	11	11	13	0	1	437
16	9	17	160	50	18	24	4	0	67	20	0	0	15	15	0	7	3	1	0	15	20	10	16	11	1	1	484
17	4	4	27	14	4	6	0	0	7	3	0	0	6	10	0	2	0	2	1	6	5	2	3	1	0	0	107
18	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
19	4	20	164	59	17	22	0	0	44	20	0	0	8	22	2	6	0	3	5	19	21	10	5	16	0	3	470
20	12	24	156	68	37	19	0	0	55	30	0	0	13	18	4	14	1	2	2	14	21	9	28	19	0	0	546
21	11	14	162	46	43	32	3	0	76	37	0	0	5	32	3	3	0	1	5	10	32	8	19	4	0	2	548
22	13	16	174	23	29	20	1	0	58	18	0	0	19	16	3	5	2	3	4	8	25	4	19	17	0	0	477
23	6	23	155	41	40	23	0	0	78	10	0	0	16	21	4	3	2	3	6	10	30	7	24	4	2	0	508
24	4	14	49	19	5	9	0	0	14	5	0	0	5	7	1	3	1	1	2	1	4	5	0	2	0	0	151
25	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
26	7	9	192	20	39	18	0	0	49	16	0	0	10	16	1	2	1	2	3	11	33	10	12	9	0	0	460
27	8	21	190	28	54	24	4	0	49	20	0	0	17	18	4	4	1	1	12	5	19	8	28	10	1	0	526
28	7	21	155	38	45	19	4	0	78	16	0	0	16	26	3	17	1	1	2	8	24	6	16	8	0	1	512
29	14	14	159	27	29	23	2	2	73	25	0	0	10	19	1	2	1	1	2	6	22	5	25	11	0	0	473
30	8	20	146	19	29	26	0	0	44	22	0	0	14	16	3	4	1	1	6	11	16	3	33	4	0	2	428
31	3	6	41	14	15	3	0	0	9	4	0	0	6	7	1	1	1	0	0	2	2	1	2	2	0	0	120

Activity Audit for

July 01 2004 Through July 31 2004

Date	Antiulcers app.	Antiulcers den.	Anxiolytic/ Hypnotics app.	Anxiolytic/ Hypnotics den.	Antihistamine app.	Antihistamine den.	Growth Hormones app.	Growth Hormones den.	Stimulant app.	Stimulant den.	Smoking Cess. app.	Smoking Cess. den.	Nsaids app.	Nsaids den.	ACE Inhibitors app.	ACE Inhibitors den.	HTN Combos app.	HTN Combos den.	Calcium Channel Blockers app.	Calcium Channel Blockers den.	Plavix app.	Plavix den.	NPA app.	NPA den.	Misc app.	Misc den.	Daily Total
App.	385		4069		733		30		1246		0		288		68		32		107		592		377		5		
Den.		485		804		520		2		458		0		497		132		45		268		156		215		19	
Average Length of Approvals in Days	34		93		97		182		261		0		346		318		334		333		270		192		201		

Smoking Cessation	0 PA's for Zyban	0 Total PA's Approved
	0 PA's for Nicotine Patch	0 Unique RID's

Changes to existing PA's	1019
Total (Previous Year)	8565

*** Denial Codes**

762 = Lack of clinical information	52.32%
763 = Medication not eligible	1.89%
764 = Existing PA	26.94%
772 = Not qualified for requested Tier	7.52%

SUPER PA's

Early Refill Attempts	79715
Dosing Change	583
lost/stolen/broke	141
Other	130
wrong DS	66
Quantity vs. Days Supply	312

Monthly Totals

	Number	Percent of Total
Approved	8025	58.10%
Additional PA's	8	0.06%
SUPER PA's	906	6.56%
Emergency PA's	3	0.02%
Duplicates	59	0.43%
Incompletes	1167	8.45%
Denied *	3645	26.39%
Total	13813	100.00%

Daily Average of 531.27 for 26 Days

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

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

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

Date Processed: Friday, September 03, 2004

Activity Audit for

August 01 2004 Through August 31 2004

Date	Antiulcers app.	Antiulcers den.	Anxiolytic/ Hypnotics app.	Anxiolytic/ Hypnotics den.	Antihistamine app.	Antihistamine den.	Growth Hormones app.	Growth Hormones den.	Stimulant app.	Stimulant den.	Smoking Cess. app.	Smoking Cess. den.	Nsaids app.	Nsaids den.	ACE Inhibitors app.	ACE Inhibitors den.	HTN Combos app.	HTN Combos den.	Calcium Channel Blockers app.	Calcium Channel Blockers den.	Plavix app.	Plavix den.	NPA app.	NPA den.	Misc app.	Misc den.	Daily Total
1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	16	16	250	46	40	18	0	1	30	8	0	0	16	23	1	6	7	2	4	6	28	5	10	12	0	0	545
3	15	24	255	34	45	19	1	1	63	26	0	0	14	25	2	9	0	1	6	24	27	7	20	15	0	2	635
4	9	22	233	44	40	21	4	0	75	15	0	0	15	30	2	7	0	6	3	14	29	7	20	10	0	0	606
5	7	22	168	22	36	16	3	0	52	18	0	0	21	27	2	5	5	3	8	10	28	5	18	8	0	1	485
6	5	22	178	27	28	20	1	0	73	20	0	0	15	16	1	4	3	2	5	12	21	15	14	12	0	3	497
7	5	6	33	9	9	12	0	0	14	6	0	0	3	11	0	2	1	2	1	4	4	3	0	1	0	1	127
8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9	7	27	175	22	43	18	0	0	48	15	1	0	14	35	2	4	1	1	7	18	28	9	14	10	1	1	501
10	8	36	180	30	33	29	5	0	84	33	0	0	11	34	0	6	6	2	3	16	17	12	19	16	0	1	581
11	2	22	175	28	31	27	5	0	79	22	0	0	12	24	1	3	1	1	5	5	29	9	9	18	0	2	510
12	7	34	155	39	27	31	0	0	90	31	0	0	16	39	3	5	4	2	14	18	26	11	12	18	0	1	583
13	7	22	143	27	35	29	1	0	107	17	0	0	12	30	0	2	1	3	4	10	23	8	28	11	0	1	521
14	0	5	40	3	5	9	0	0	19	11	0	0	2	7	1	2	0	1	2	4	7	1	1	2	0	0	122
15	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
17	13	47	277	66	65	46	1	1	156	53	0	0	13	44	3	12	1	8	12	16	29	15	29	24	0	2	933
18	8	23	222	32	44	21	0	0	83	29	0	0	10	26	2	6	2	0	4	15	28	12	17	17	0	3	604
19	3	12	123	34	27	26	5	0	70	24	0	0	19	34	4	3	1	1	7	13	19	4	21	13	0	1	464
20	2	21	138	39	47	26	0	0	88	24	0	0	21	23	2	3	1	2	6	10	24	12	24	6	0	0	519
21	0	4	33	6	8	6	0	0	25	15	0	0	0	4	1	1	0	0	1	1	3	2	1	2	0	0	113
22	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
23	5	11	129	17	21	19	0	0	32	15	0	0	6	17	1	2	0	2	3	3	18	3	25	6	0	3	338
24	8	27	198	54	65	39	0	0	84	46	0	0	15	40	1	11	1	5	4	15	26	26	30	25	0	1	721
25	3	18	154	32	33	24	6	0	101	34	0	0	13	22	1	4	1	1	3	7	22	5	27	14	0	3	528
26	4	24	161	19	37	26	0	0	67	15	0	0	7	21	3	6	1	2	4	11	22	9	20	15	1	3	478
27	8	10	124	24	35	8	9	0	62	17	0	0	14	10	2	7	2	1	4	12	15	2	37	10	0	0	413
28	3	6	52	15	22	20	0	0	40	10	0	0	10	8	1	0	2	0	0	5	6	3	0	2	1	0	206
29	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
30	3	13	136	19	42	13	2	0	60	25	0	0	8	9	1	4	2	0	2	10	19	1	27	10	0	0	406
31	3	27	175	16	57	25	0	0	94	43	0	0	18	29	0	11	0	5	4	9	19	10	27	11	1	0	584

Activity Audit for

August 01 2004 Through August 31 2004

Date	Antiulcers app.	Antiulcers den.	Anxiolytic/ Hypnotics app.	Anxiolytic/ Hypnotics den.	Antihistamine app.	Antihistamine den.	Growth Hormones app.	Growth Hormones den.	Stimulant app.	Stimulant den.	Smoking Cess. app.	Smoking Cess. den.	Nsaids app.	Nsaids den.	ACE Inhibitors app.	ACE Inhibitors den.	HTN Combos app.	HTN Combos den.	Calcium Channel Blockers app.	Calcium Channel Blockers den.	Plavix app.	Plavix den.	NPA app.	NPA den.	Misc app.	Misc den.	Daily Total
App.	151		3907		875		43		1696		1		305		37		43		116		517		450		4		
Den.		501		704		548		3		572		0		588		125		53		268		196		288		29	
Average Length of Approvals in Days	89		94		95		160		267		0		342		336		357		338		270		184		64		

Smoking Cessation	0 PA's for Zyban	1 Total PA's Approved
	1 PA's for Nicotine Patch	1 Unique RID's

*** Denial Codes**

762 = Lack of clinical information	59.03%
763 = Medication not eligible	1.59%
764 = Existing PA	20.10%
772 = Not qualified for requested Tier	7.53%

Changes to existing PA's	45
Total (Previous Year)	10213

SUPER PA's

Early Refill Attempts	59511
Dosing Change	666
lost/stolen/broke	149
Other	136
wrong DS	77
Quantity vs. Days Supply	577

Monthly Totals

	Number	Percent of Total
Approved	8191	50.77%
Additional PA's	6	0.04%
SUPER PA's	1605	9.95%
Emergency PA's	8	0.05%
Duplicates	1221	7.57%
Incompletes	1196	7.41%
Denied *	3905	24.21%
Total	16132	100.00%

Daily Average of 620.46 for 26 Days

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

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

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

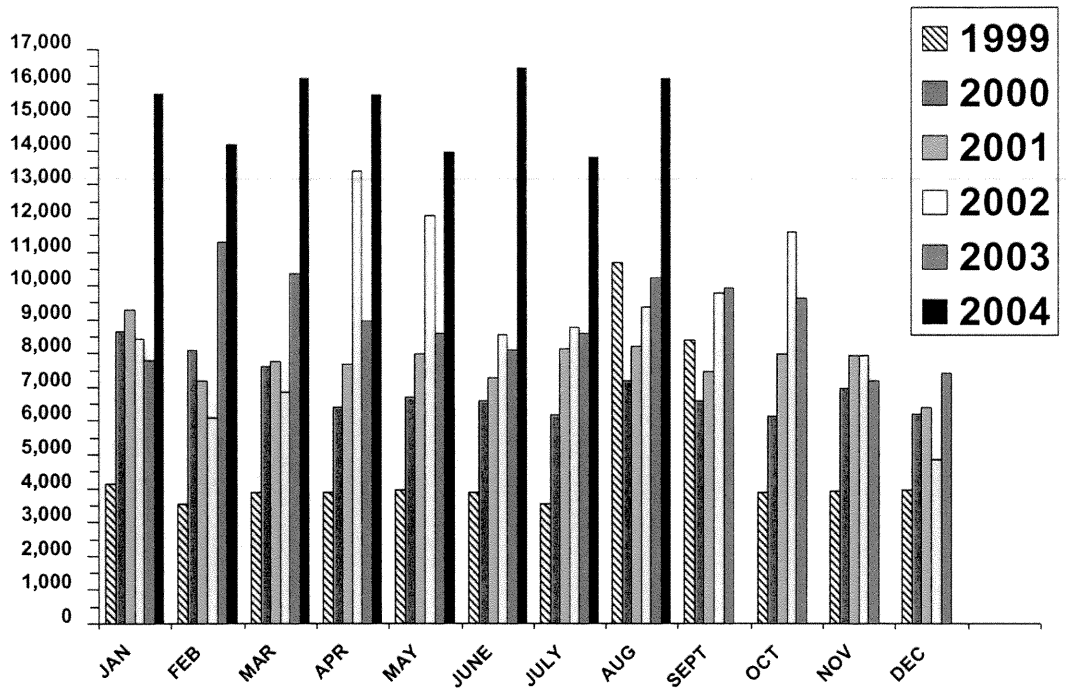
PRIOR AUTHORIZATION ACTIVITY AUDIT

Monthly Totals

MONTH	1999 Total *(approved/ duplicates/ denied)*	2000 Total *(approved/ duplicates/ denied)*	2001 Total *(approved/ duplicates/ denied)*	2002 Total *(approved/ duplicates/ denied)*	2003 Total *(approved/ duplicates/ denied)*	2004 Total *(approved/ duplicates/ denied)*
January	4,124	8,669	9,296	8,427	7,797	15,688
February	3,542	8,077	7,194	6,095	11,272	14,188
March	3,856	7,588	7,748	6,833	10,358	16,138
April	3,867	6,390	7,676	13,381	8,953	15,644
May	3,959	6,711	7,980	12,082	8,589	13,960
June	3,884	6,565	7,249	8,550	8,084	16,454
July	3,523	6,181	8,133	8,775	8,565	13,813
August	10,676	7,183	8,195	9,353	10,213	16,132
September	8,387	6,585	7,438	9,793	9,918	
October	3,863	6,140	7,956	11,584	9,615	
November	3,919	6,961	7,949	7,921	7,201	
December	3,953	6,206	6,385	4,867	7,391	
Calendar Year Total	**57,553**	**83,256**	**93,199**	**107,661**	**107,956**	**122,017**

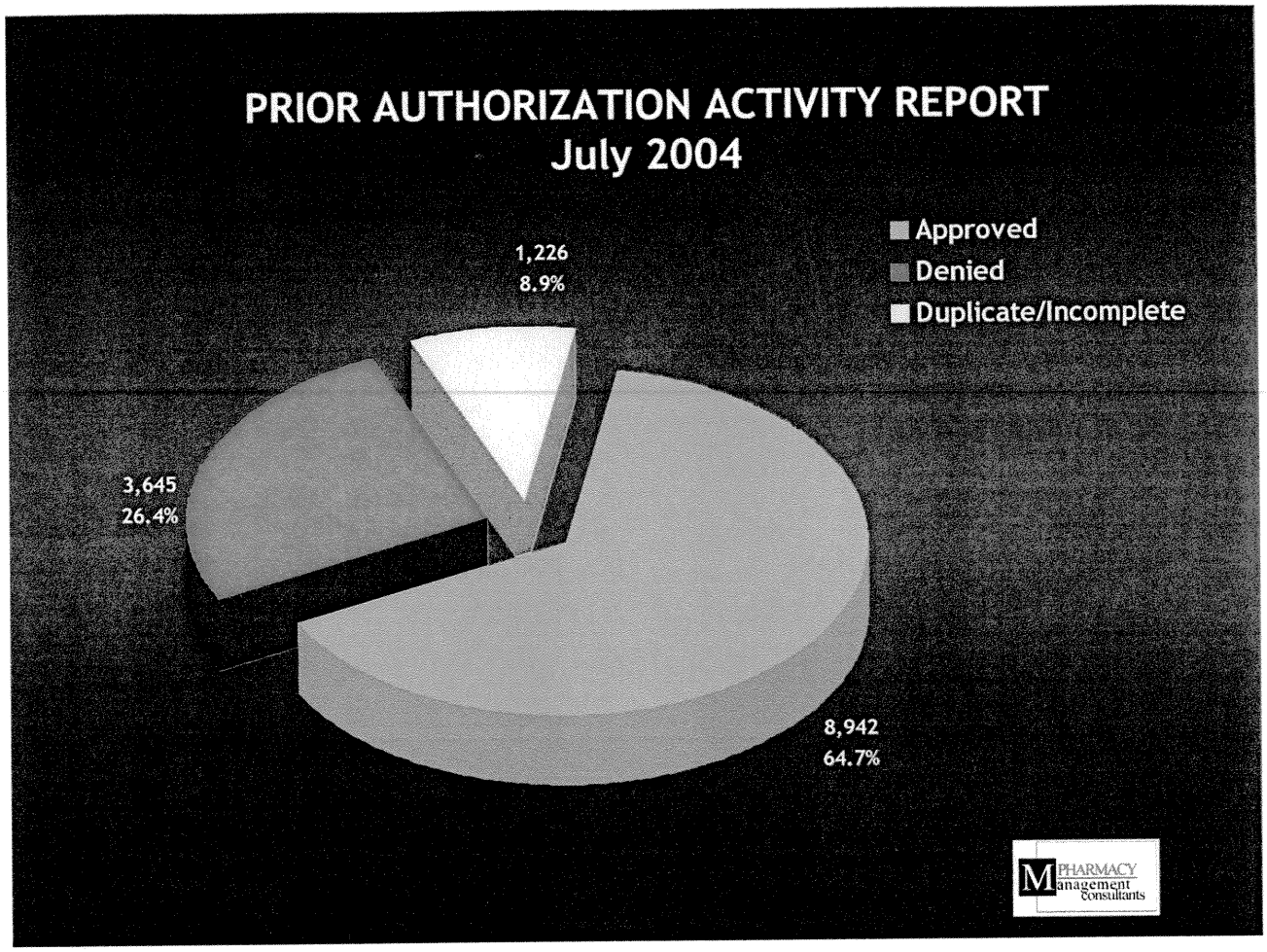
Monthly PA Activity

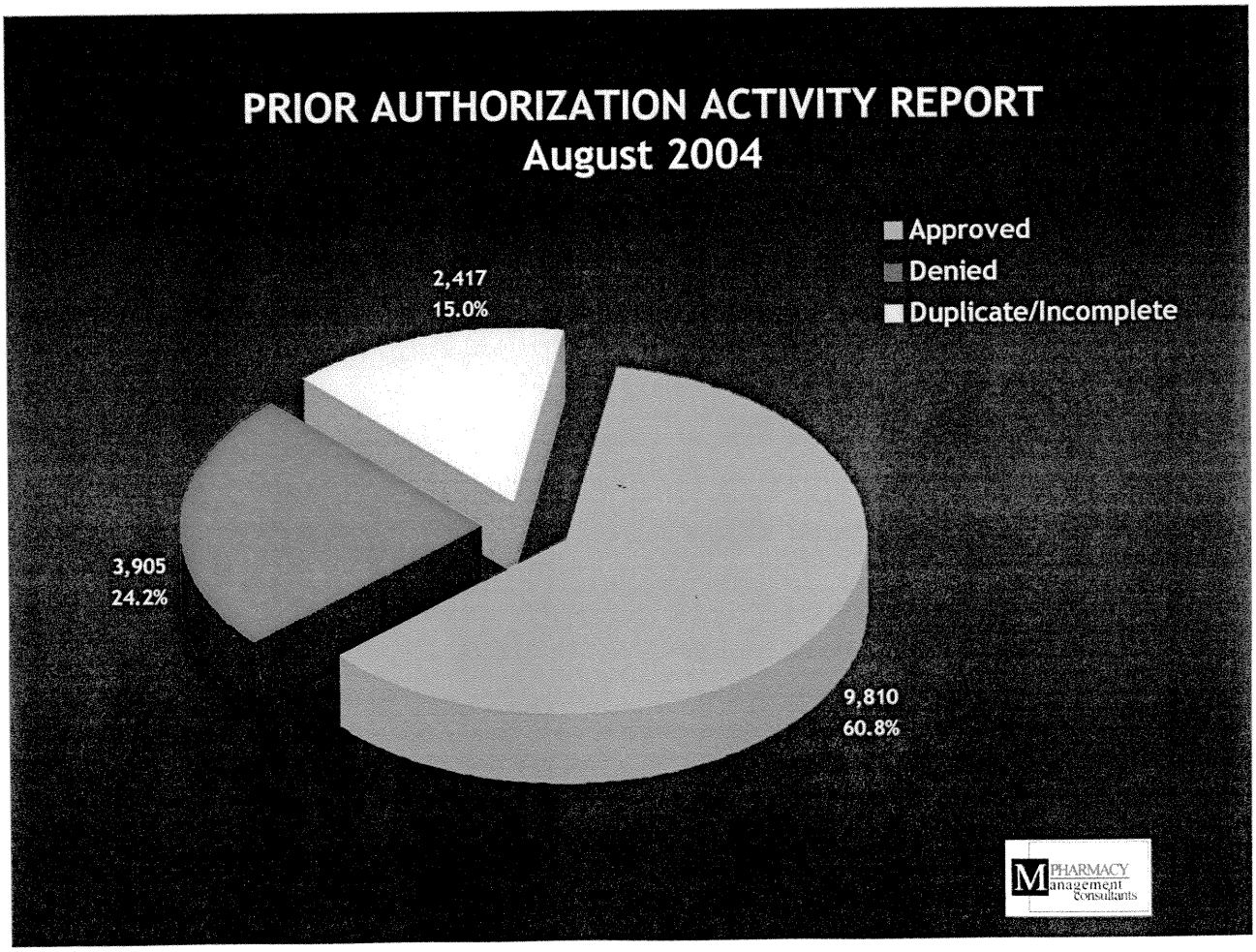
Calendar Years 2000-2004

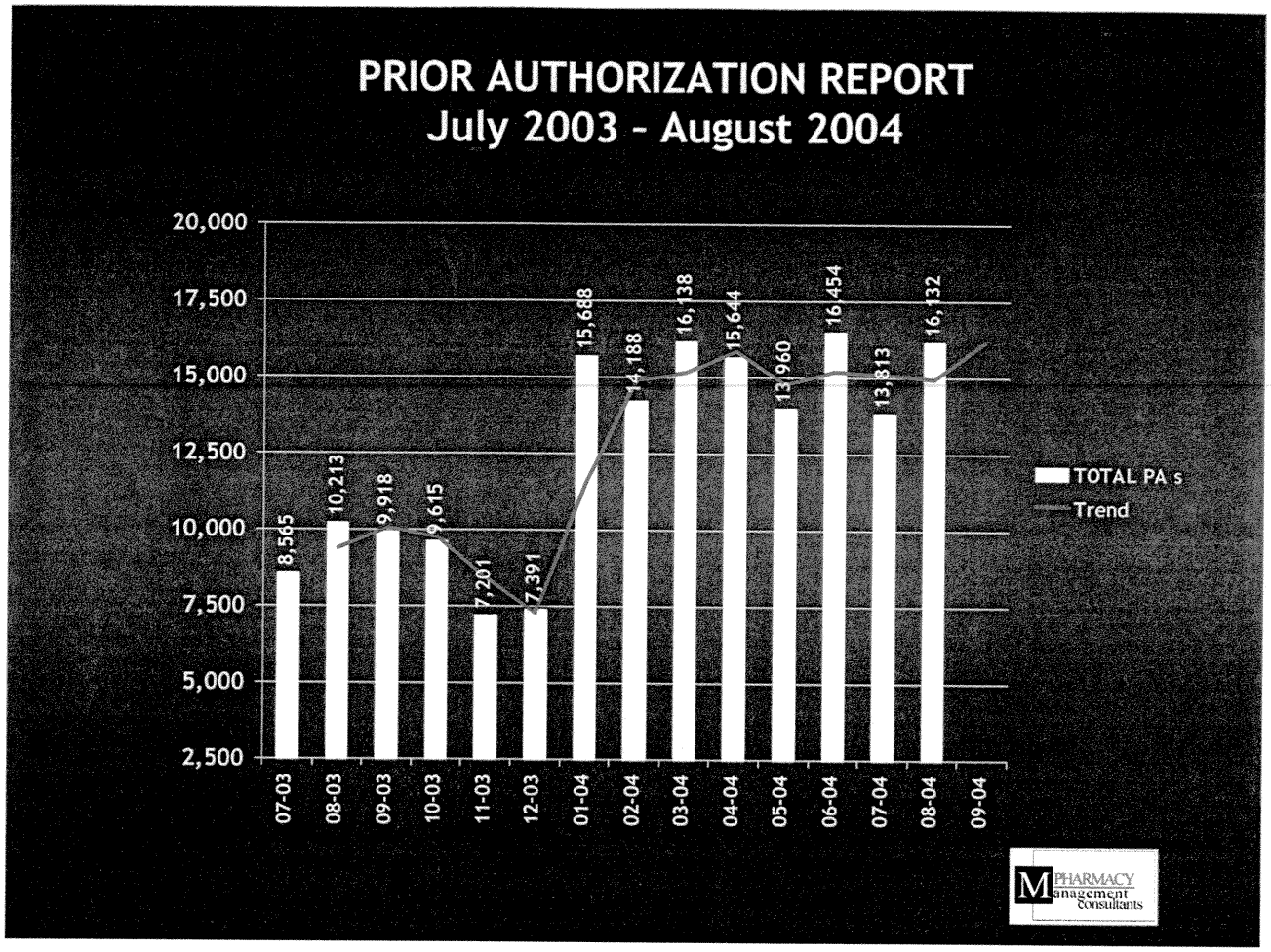


Monthly PA Activity

Calendar Years 2000-2004


PRIOR AUTHORIZATION ACTIVITY REPORT
July 2004
Approved
Denied
Duplicate/Incomplete
1,226
8.9%
3,645
26.4%
8,942
64.7%
PHARMACY Management Consultants


PRIOR AUTHORIZATION ACTIVITY REPORT
August 2004
Approved
Denied
Duplicate/Incomplete
2,417
15.0%
3,905
24.2%
9,810
60.8%
PHARMACY Management Consultants


PRIOR AUTHORIZATION REPORT
July 2003 - August 2004
20,000
17,500
15,000
12,500
10,000
7,500
5,000
2,500
8,565
10,213
9,918
9,615
7,201
7,391
15,688
14,188
16,138
15,644
13,960
16,454
13,813
16,132
07-03
08-03
09-03
10-03
11-03
12-03
01-04
02-04
03-04
04-04
05-04
06-04
07-04
08-04
09-04
TOTAL PA's
Trend
PHARMACY Management Consultants

CALL VOLUME -JULY 2004

JULY 04	CALLER					ISSUE					TYPE OF CALL					RESOLUTION							
																	Resolved						
	Call Volume	Physician	Pharmacies	Clients	Other	Eligibility	Claims	PA Issue	SMAC	Other	Regular	Callback	Proactive	ProDUR	Other	Helpdesk Resolved	Transferred Pharmacist	Transferred Supervisor	OHCA	Reversals/ Adjustments	EDS	Customer Service	Provider Contracts
1	1000	9	859	83	49	130	485	107	0	278	936	25	0	31	8	993	1	0	0	2	0	4	0
2	771	0	697	62	12	144	305	73	0	249	735	7	1	27	1	765	0	2	0	0	0	4	0
3	176	0	166	6	4	27	84	14	0	51	168	2	0	5	1	176	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6	756	9	666	65	16	92	335	89	0	240	731	10	2	7	6	742	2	2	0	2	0	8	0
7	757	19	661	48	29	181	285	98	0	193	703	16	2	28	8	739	4	2	7	1	0	4	0
8	717	10	634	62	11	171	307	75	0	164	687	4	0	21	5	703	3	1	6	1	0	3	0
9	682	18	579	65	20	114	258	102	0	208	655	5	0	15	7	662	7	0	0	3	1	9	0
10	146	0	134	10	2	33	67	14	0	32	141	1	0	3	1	144	0	0	0	2	0	0	0
11	42	0	39	1	2	6	25	2	0	9	36	0	0	4	2	42	0	0	0	0	0	0	0
12	731	12	628	72	19	111	346	87	0	187	716	2	4	6	3	731	0	0	0	0	0	0	0
13	683	14	586	51	32	129	257	81	0	216	640	21	3	16	2	675	1	5	1	0	0	3	0
14	632	5	567	39	21	163	218	49	0	202	611	6	0	8	6	622	1	2	1	0	0	6	0
15	767	11	670	52	34	267	204	100	0	196	740	11	0	9	7	751	4	9	2	1	0	0	0
16	703	6	628	53	16	100	314	110	0	179	663	12	2	21	5	683	6	1	0	0	0	12	0
17	174	0	167	4	3	26	108	8	0	32	161	0	2	10	1	173	0	0	0	1	0	1	0
18	66	0	65	0	1	17	43	0	0	6	63	1	0	2	0	65	0	0	0	1	0	0	0
19	892	13	794	61	24	124	430	125	0	213	860	9	4	17	2	870	1	4	1	0	0	16	0
20	829	20	718	57	34	110	401	119	0	199	796	20	2	9	2	814	3	0	0	2	0	8	0
21	758	18	664	51	25	97	321	135	0	205	727	16	0	12	3	736	7	1	1	1	0	12	1
22	667	23	564	57	23	83	288	90	0	206	644	9	0	9	5	641	3	3	0	0	0	16	1
23	641	13	557	49	22	70	307	90	0	174	604	6	3	22	6	626	4	1	0	0	0	8	0
24	149	0	139	5	5	17	76	6	1	49	137	1	1	9	1	149	0	0	0	0	0	0	0
25	42	0	40	2	0	4	26	1	0	11	39	0	0	2	1	41	0	0	0	0	0	1	0
26	825	17	738	48	22	125	385	87	2	226	796	12	0	10	7	812	3	1	0	2	0	7	0
27	760	26	630	67	37	94	331	103	0	230	729	18	1	6	6	742	3	1	2	0	0	12	0
28	760	19	667	51	23	78	369	95	0	218	740	6	3	7	4	744	3	0	1	1	1	10	0
29	741	14	654	57	16	91	374	98	0	178	723	7	1	7	3	733	1	0	0	0	0	7	0
30	616	18	531	50	17	63	279	88	0	186	594	7	0	10	5	596	4	3	2	0	0	9	0
31	179	0	176	3	0	31	87	9	0	52	179	0	0	0	0	179	0	0	0	0	0	0	0
Total	**16,662**	**294**	**14,618**	**1,231**	**519**	**2,698**	**7,315**	**2,055**	**3**	**4,589**	**15,954**	**234**	**31**	**333**	**108**	**16,349**	**61**	**38**	**24**	**20**	**2**	**160**	**2**
ercentage	**100.00%**	**1.76%**	**87.73%**	**7.39%**	**3.11%**	**16.19%**	**43.90%**	**12.33%**	**0.02%**	**27.54%**	**95.75%**	**1.40%**	**0.19%**	**2.00%**	**0.65%**	**98.12%**	**0.37%**	**0.23%**	**0.14%**	**0.12%**	**0.01%**	**0.96%**	**0.01%**

CALL VOLUME -AUGUST 2004

AUGUST 04	CALLER					ISSUE					TYPE OF CALL					RESOLUTION							
																	Resolved						
	Call Volume	Physician	Pharmacies	Clients	Other	Eligibility	Claims	PA Issue	SMAC	Other	Regular	Callback	Proactive	ProDUR	Other	Helpdesk Resolved	Transferred Pharmacist	Transferred Supervisor	OHCA	Reversals/ Adjustments	EDS	Customer Service	Provider Contracts
1	88	0	87	1	0	14	60	2	0	12	88	0	0	0	0	88	0	0	0	0	0	0	0
2	973	8	878	57	30	162	444	72	0	294	941	2	19	11	3	956	4	1	9	1	1	0	0
3	900	7	720	52	131	198	260	94	0	347	748	4	122	20	6	883	4	3	5	2	0	3	0
4	742	8	577	42	115	104	265	78	0	295	528	11	180	18	5	740	0	2	0	0	0	0	0
5	730	11	656	40	23	221	205	80	0	224	710	11	4	4	1	712	3	2	0	2	0	10	0
6	602	10	532	53	7	91	246	77	0	187	594	3	0	3	2	594	3	5	0	0	0	0	0
7	169	0	158	4	7	15	93	15	0	46	155	0	1	9	4	169	0	0	0	0	0	0	0
8	46	0	44	1	1	4	28	2	0	12	51	0	0	3	1	46	0	0	0	0	0	0	0
9	754	21	654	55	24	103	344	86	0	220	724	8	1	13	8	743	4	6	0	0	0	1	0
10	730	25	624	63	18	171	252	87	0	218	709	11	1	8	1	715	6	3	0	0	0	6	0
11	771	17	649	83	22	94	315	122	0	240	774	5	5	12	4	753	3	6	1	0	0	8	0
12	624	15	535	60	14	76	290	87	0	170	602	9	0	10	2	612	1	6	0	0	0	5	0
13	679	7	592	59	21	72	318	105	1	183	647	6	0	18	7	661	2	0	2	0	0	11	0
14	150	0	144	5	1	28	64	13	0	45	148	1	0	1	0	150	0	0	0	0	0	0	0
15	51	0	51	0	0	11	32	0	0	8	46	0	0	5	0	51	0	0	0	0	0	0	0
16	712	0	694	18	0	6	1	8	0	697	712	0	0	0	0	711	0	0	0	0	0	1	0
17	903	20	783	82	18	119	389	128	0	266	872	5	1	19	6	881	8	0	1	2	0	10	0
18	754	21	664	57	12	99	326	103	0	225	724	16	1	9	4	736	6	4	0	0	0	8	0
19	707	14	700	72	21	99	312	88	0	207	685	14	1	1	6	690	3	1	3	9	0	0	0
20	675	2	592	71	10	158	240	67	0	210	660	1	0	3	3	663	3	3	0	1	0	5	0
21	157	0	147	3	7	41	56	15	0	45	148	3	0	3	3	156	0	0	0	0	0	1	0
22	67	0	65	1	1	33	18	2	0	14	65	0	1	1	0	67	0	0	0	0	0	0	0
23	755	13	657	65	20	91	374	89	0	201	729	8	0	11	6	740	3	0	2	0	0	10	0
24	777	16	656	74	31	75	372	104	0	224	745	18	1	6	6	753	3	3	1	5	0	11	0
25	765	12	663	75	15	103	321	102	0	239	738	9	1	9	5	750	5	0	0	2	0	8	0
26	916	7	819	68	22	91	405	80	0	340	884	9	0	16	7	899	2	2	0	4	0	9	0
27	683	5	588	72	18	80	318	84	0	197	667	0	1	8	7	674	5	0	0	0	0	4	0
28	170	0	160	5	5	29	89	14	0	38	162	1	0	3	4	170	0	0	0	0	0	0	0
29	63	0	61	2	0	25	32	1	0	5	59	0	0	4	0	62	0	0	0	0	0	1	0
30	695	10	625	45	15	80	429	45	0	141	684	2	1	5	3	689	2	1	0	0	0	3	0
31	755	11	481	46	15	155	395	65	0	146	743	3	3	4	8	750	5	6	0	0	0	0	0
Total	**17,563**	**260**	**15,256**	**1,331**	**624**	**2,648**	**7,293**	**1,915**	**1**	**5,696**	**16,742**	**160**	**344**	**237**	**112**	**17,264**	**75**	**54**	**24**	**28**	**1**	**115**	**0**
Percentage	**100.00%**	**1.48%**	**86.86%**	**7.58%**	**3.55%**	**15.08%**	**41.52%**	**10.90%**	**0.01%**	**32.43%**	**95.33%**	**0.91%**	**1.96%**	**1.35%**	**0.64%**	**98.30%**	**0.43%**	**0.31%**	**0.14%**	**0.16%**	**0.01%**	**0.65%**	**0.00%**

2nd : increased call volume due to Eckerds changing to CVS
2nd & 3rd: proactive phone calls for NABP numbers
16th: computers down all day

CALL VOLUME

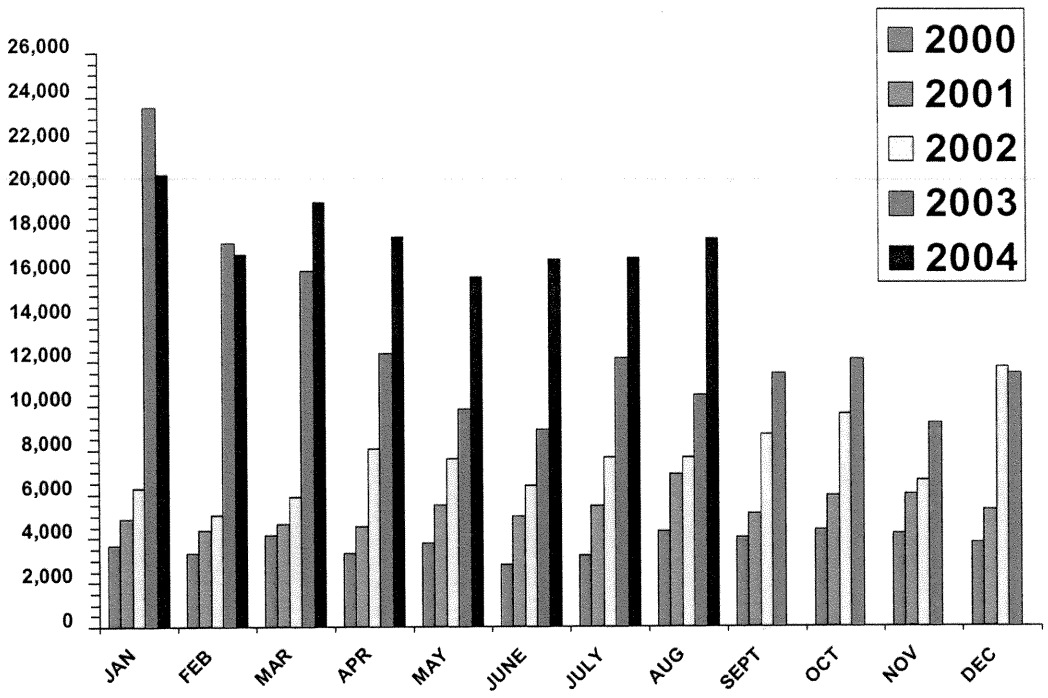
Monthly Totals

MONTH	1999 Total	2000 Total	2001 Total	2002 Total	2003 Total	2004 Total
January	* 0	3,697	4,905	6,295	23,499	20,498
February	* 0	3,335	4,393	5,049	17,354	16,857
March	* 0	4,157	4,668	5,858	16,081	19,232
April	* 0	3,337	4,556	8,047	12,378	17,660
May	* 0	3,804	5,540	7,586	9,836	15,828
June	* 0	2,820	4,982	6,368	8,917	16,634
July	* 0	3,242	5,465	7,651	12,126	16,662
August	3,883	4,333	6,881	7,629	10,454	17,563
September	2,360	4,015	5,145	8,664	11,449	
October	1,963	4,398	5,912	9,608	12,102	
November	1,721	4,216	6,011	6,627	9,178	
December	2,475	3,804	5,314	11,710	11,461	
Calendar Year Total	**12,402**	**45,158**	**63,772**	**91,092**	**154,835**	**140,934**

* Help Desk Call Center implemented in August 1999.

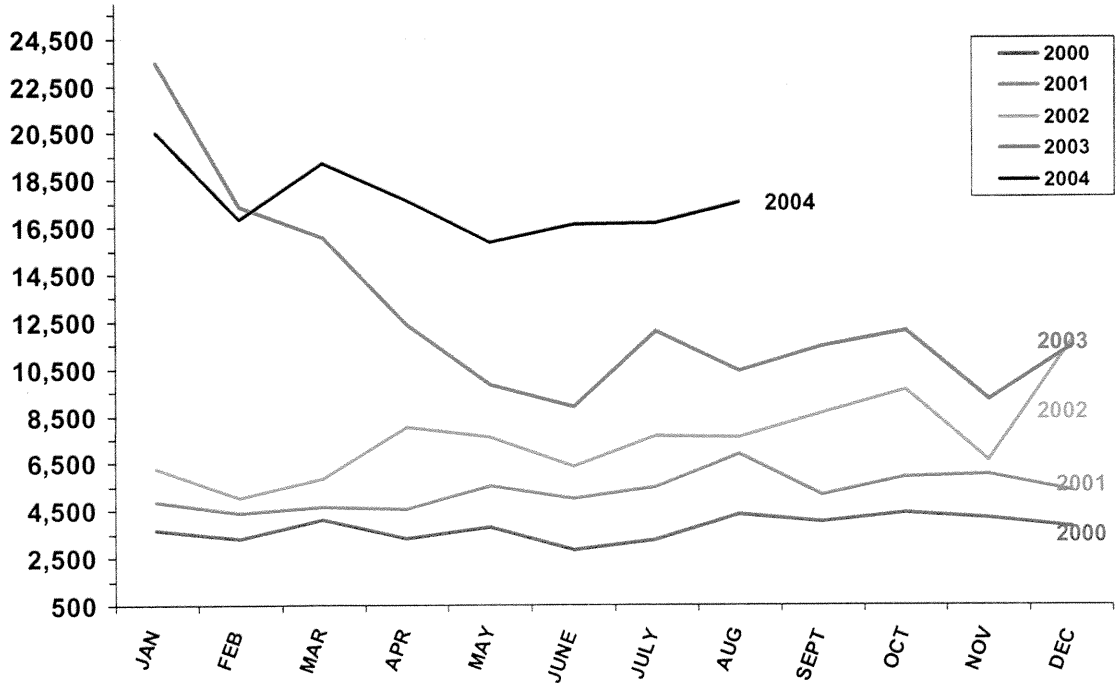
Monthly Call Volume

Calendar Years 2000-2004

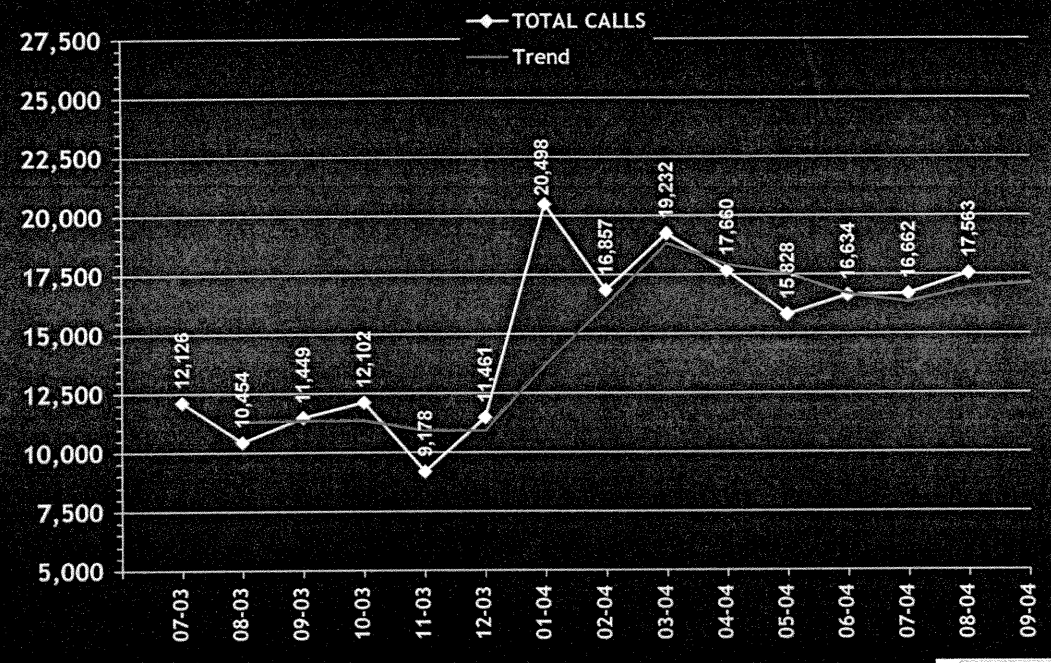


Monthly Call Volume

Calendar Years 2000-2004

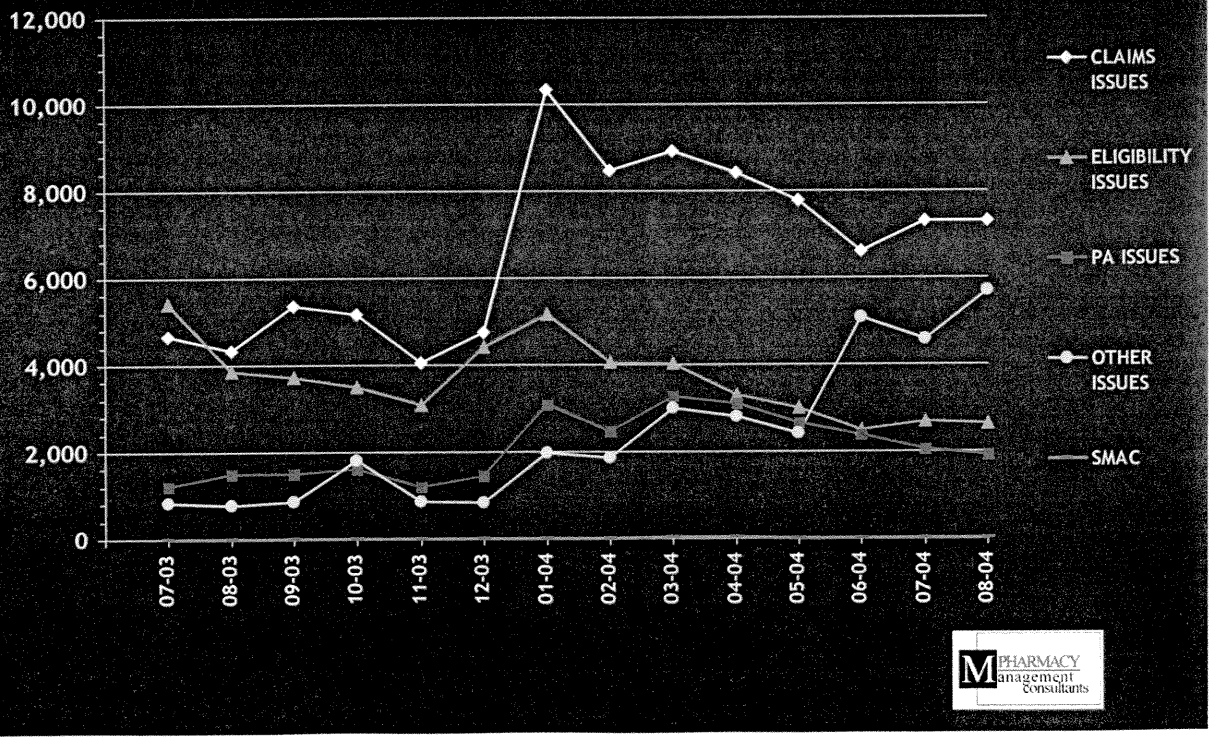


CALL VOLUME MONTHLY REPORT
July 2003 - August 2004



PHARMACY Management Consultants

CALL VOLUME ISSUES
July 2003 - August 2004



PHARMACY Management Consultants

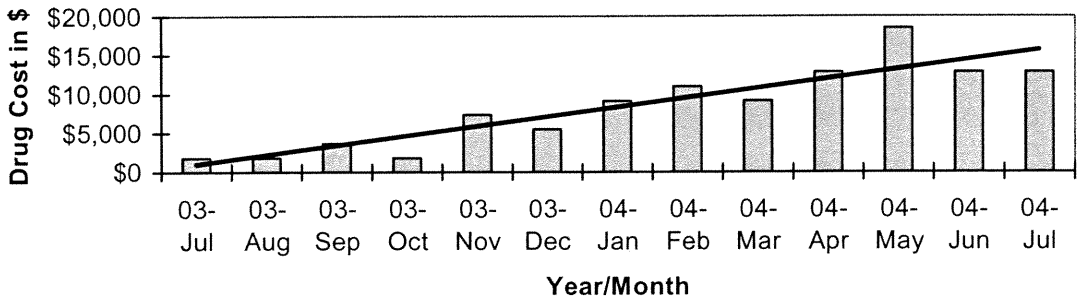
APPENDIX C

Utilization

For the period of Jan 2003 through July 2004, a total of 10 clients (1 female, 9 males) received enfuvirtide through the Medicaid fee-for-service program. These claims were prescribed by 4 prescribers, at least 2 of whom were infectious disease specialists. All but two of the patients who were started on the drug are still filling prescriptions for it.

Product	# of Claims	Total Units	Total Days	Total Cost
Fuzeon Convenience Kit (60 single-use vials, with sterile water, syringes, & alcohol wipes = 30 days of medication per kit)	**58**	**117**	**1,728**	**$106,534.49**

Cost Trend by Month



Recommendations

Proposed Oklahoma Medicaid criteria for prior authorization of Fuzeon:

- If the patient is already using Fuzeon, patient will be approved for coverage, even if he/she does not otherwise meet the criteria for approval. Coverage would be for 6 months (including however long the patient has already been using Fuzeon) and renewals would be subject to the conditions described below.
- If the patient is new to Fuzeon therapy, the patient must meet <u>all</u> of the following conditions for coverage:
  - ◊ Age > 5 yrs
  - ◊ Stable on and compliant with his/her current combination antiretroviral therapy for at least the previous 4 weeks.
  - ◊ Plasma HIV-1 RNA level of at least 5,000 copies per mL or more, from 2 samples drawn about 4 weeks apart, with the last sample being drawn within the last month, while on the current HAART. This demonstrates that the patient's current combination antiretroviral therapy is not working.

- ◊ CD4 count of 200 cells/mL or fewer, from 2 samples drawn about 4 weeks apart, with the last sample being drawn within the last 3 months, while on the current HAART. This also demonstrates that the patient's current combination antiretroviral therapy is not working.
- ◊ Client has a treatment history of use of antiretroviral drugs for at least 12 months. HIV resistance testing within the last 6 months, done while the patient was taking his/her current combination antiretroviral therapy, revealed 2 to 4 active drugs with which to construct an antiretroviral regimen for the patient. If resistance testing has not been done, prescriber must provide a detailed treatment history &/or other clinical information to justify Fuzeon use. If treatment history is used in place of resistance testing, patient must have had virologic failure or unacceptable adverse events after at least 12 months of treatment with at least 1 NRTI, at least 1 NNRTI, & at least 1 PI. Such treatment history should include a clear accounting of what drugs the patient tried and the dates they were tried, the client's response to them, and what steps were taken to determine compliance with the drugs.
- ◊ Patient is to remain on other antiretroviral medications along with the Fuzeon.
- ◊ Fuzeon dosing is appropriate per the manufacturer's recommended dosing in the product package information.

- Coverage of Fuzeon will be approved for 6 months. At the end of each approval period, prescriber must provide new plasma RNA measurements in order to show that the Fuzeon is providing benefit (plasma RNA measurements should be taken 4-8 weeks after adding the Fuzeon and then every 3 months thereafter). At the end of the first approval period, there should be at least a 1 log (10-fold) decrease in plasma RNA measurement to indicate that the Fuzeon is working.

References

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Oklahoma Medicaid Prescription Drug Program
Statement of Medical Necessity for Fuzeon® (enfuvirtide)

Pharmacy Management Consultants
Prior Authorization Unit

Phone: 405-271-6349 or 1-800-831-8921
Fax: 405-271-4014 or 800-224-4014

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After completing this form, please **fax** this form along with a completed prior authorization form and the requested documentation to Pharmacy Management Consultants. Please make sure that the client's Medicaid ID Number is on every page faxed.

PART 1: TO BE COMPLETED BY PRESCRIBER

PRESCRIBER INFORMATION	PATIENT INFORMATION
Prescriber Name:	Patient's Medicaid Client ID Number:
Address:	Patient Name:
City: State: Zip:	Address:
Phone ( )	City: State: Zip:
FAX ( )	Patient's date of birth: / /

1. **Is this patient currently receiving Fuzeon?** ❑ **Yes** ❑ **No**
   If yes, please list date the patient begin Fuzeon treatment: _____, **and please list baseline (prior to start of Fuzeon) CD4 (cells/mL) and plasma HIV-1 RNA (copies/mL):** _____
   _____
2. **Please list the patient's two most recent laboratory test results:**

Date	CD4 (cells/mL)	Plasma HIV-1 RNA (copies/mL)
_____	_____	_____
_____	_____	_____

   If the CD4 count is > 200 cells/mL or the plasma HIV-1 RNA is < 5000 copies/mL, please provide further justification for Fuzeon use: _____
   _____
3. **Has HIV resistance testing been obtained within the past 6 months, while the patient has been taking his/her current antiretroviral drug regimen?** ❑ **Yes** ❑ **No**
4. **According to the HIV resistance test results, are there at least 2 but no more than 4 active drugs with which to construct an antiretroviral drug regimen for this patient?** ❑ **Yes** ❑ **No**
5. **Please provide documentation of 3-class antiretroviral drug resistance, including copies of genotype/phenotype. If resistance test results are not available, please provide further justification for Fuzeon use (detailed treatment history, etc.).** _____
   _____
   _____
6. **Please provide proposed antiretroviral treatment regimen** (please add add'l pages if needed, with ID# on each page):
   _____
   _____
7. **Fuzeon dose:** ❑ **90 mg SC BID** ❑ **Other (specify)** _____
   Please explain rationale for dose other than Fuzeon 90 mg SC BID: _____
8. **The patient has been educated about storage and administration of Fuzeon, and sharps disposal.** ❑ **Yes** ❑ **No**

Prescriber Signature: _____ **Date:** _____

(With this signature, the prescriber confirms that the information above is accurate and verifiable in patient records.)

APPENDIX D

Xopenex® (levalbuterol) Utilization
June 2003 to May 2004
Oklahoma Medicaid
September 2004

Current Limitations/Restrictions on Xopenex®
Quantity limit: 288ml/30days (32 days of tid dosing). No current limitations on client age.

NAEPP Asthma Guidelines (see attached Quick Reference) [1]
The guidelines were revised in July 2002. This revision made inhaled corticosteroids the preferred treatment for long-term control of all types of asthma, except for mild intermittent asthma. Bronchodilators, theophylline, and leukotriene agents are either adjunctive or alternate choices.

GOLD Recommendations[2]
The Global Initiative for Chronic Obstructive Lung Disease recommendations were revised March 2004. Pharmacological treatment is based upon the stage COPD progression. First, as needed bronchodilators are used. Then as the disease progresses, routine use of long-acting bronchodilators are added. Later, inhaled corticosteroids are used if the patient experiences routine exacerbations.

What is Xopenex® (levalbuterol)?
Levalbuterol is the R-enantiomer of racemic albuterol. This enantiomer is responsible for all bronchodilating activity of commercially available albuterol. Levalbuterol has a higher binding affinity than racemic albuterol.[3] The long standing assumption that S-albuterol does not have any physiological effect is currently being questioned in both research and the literature. S-albuterol is metabolized slower than R-albuterol and in vitro studies have shown this to have potentially negative effects. The proposed advantage of levalbuterol, being a pure isomer, is that it is thought to be "safer" than racemic albuterol. This is a very controversial issue; there are articles and trials in the literature to support both sides of the debate. Where this possible safety issue would be most important is when repeated dosing of albuterol is required. This repeated dosing, if the prescriber is following NAEPP[1] or GOLD[2] guidelines, would occur during an asthma exacerbation or for treating COPD.

Xopenex® is approved for the treatment of bronchospasm in adults, adolescents and children 6 years of age and older with reversible obstructive airway disease.[3]

The recommended dose for those from 6-11 years of age is 0.31mg administered via nebulization three times a day; routine dosing ***not to exceed 0.63mg three times a day***.[3]

The recommended dose for those 12 years of age and up is 0.63mg administered three times a day, every 6-8 hours. Those not responding adequately to this dose may be moved up to 1.25mg three times a day.[3]

Appendix A-2 of the NAEPP Guidelines[1] lists the dosing for levalbuterol used for "quick relief" for children under 12 years as 0.025mg/kg (min 0.63mg, max 1.25mg) every 4-8 hours. Dosing for those 12 years of age and up is 0.63mg-2.5mg every 4-8 hours. NAEPP dosing for the treatment of exacerbations in the Emergency Department or Hospital is much more aggressive since the patient is continually monitored for adverse effects.

Utilization – June 2003 to May 2004

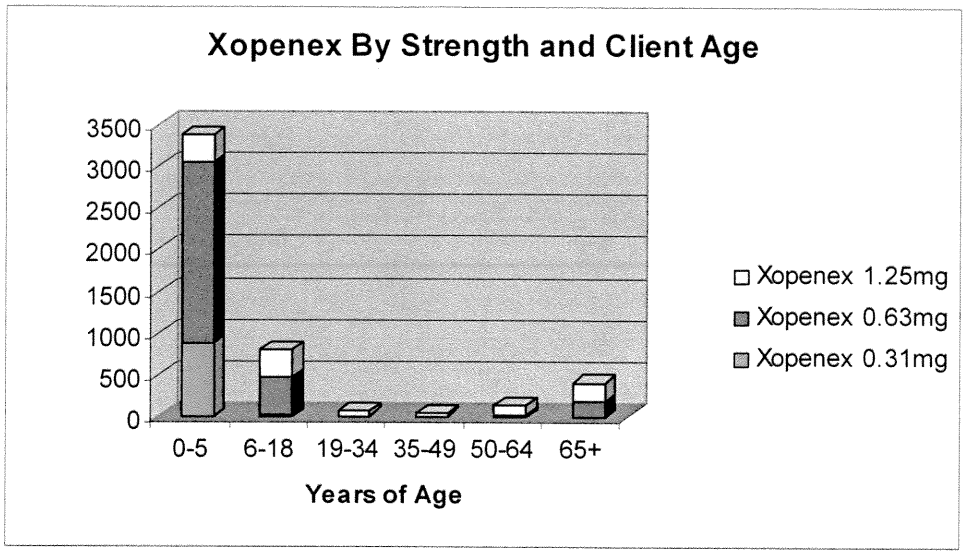
For the period of June 2003 to May 2004 a total of 4,898 clients received Xopenex® through the Medicaid fee-for-service program.

Drug	Claims	Total Units	Total Days	Total Cost	Total Clients	Per Diem
Xopenex® 0.31mg/3ml	1,516	253,838	26,459	$200,899.51	908	$7.59
Xopenex® 0.63mg/3ml	6,200	926,747	90,427	$725,476.11	3,033	$8.02
Xopenex® 1.25mg/3ml	3,460	552,591	45,472	$431,508.11	1,241	$9.49
Totals	**11,176**	**1,733,176**	**162,358**	**$1,357,883.73**	**4,898***	**$8.36**

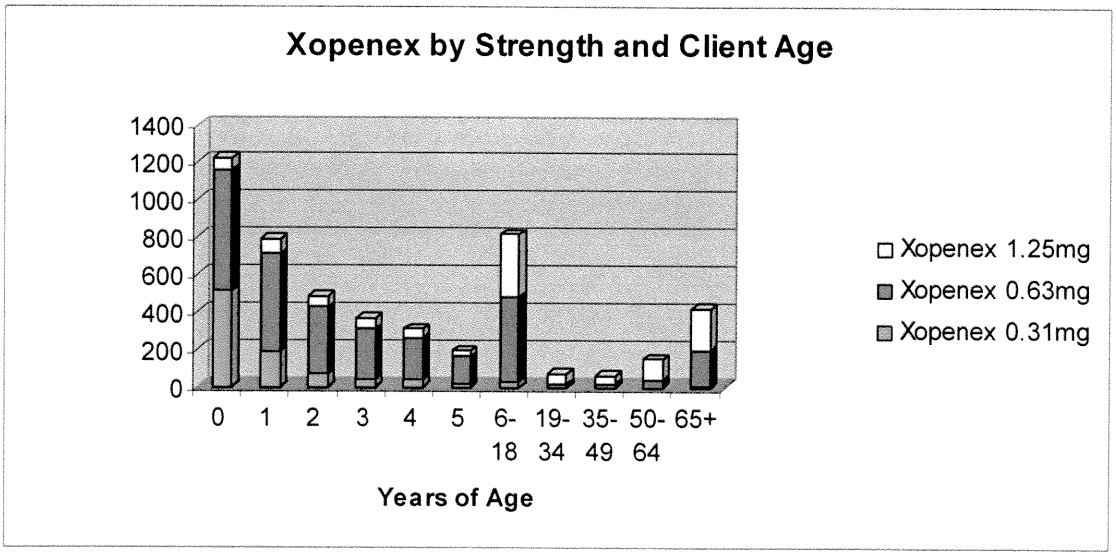
*Total number of non-duplicated clients

Total Cost 12 month period	**$1,357,883.73**	**+64.8%**
Total Cost Previous 12 months	$823,535.40	
Total Claims 12 month period	**11,176**	**+41.0%**
Total Claims Previous 12 months	7,923	
Total Clients 12 month period	**4,898**	**+60.1%**
Total Claims Previous 12 months	3,048	
Per Diem 12 month period	**$8.36**	**+6.8%**
Per Diem Previous 12 months	$7.83	

Claims were reviewed to determine the number of clients by age and drug strength. As you can see from the chart below, sixty-nine percent (69%) of the Xopenex use is in clients under the approved age of 6 years.

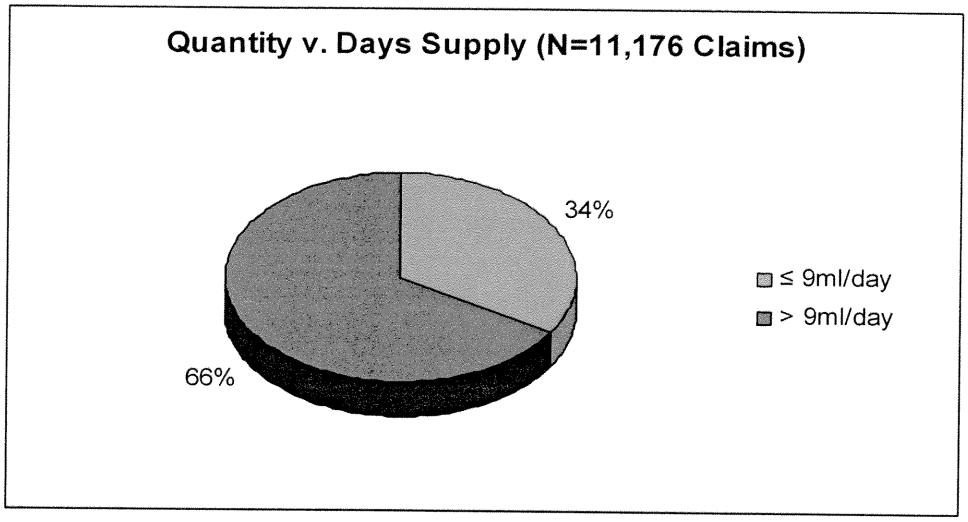


If the age range for the pediatric population is expanded, the utilization chart shows that twenty-five percent (25%) of utilization is in clients under the age of 12 months.

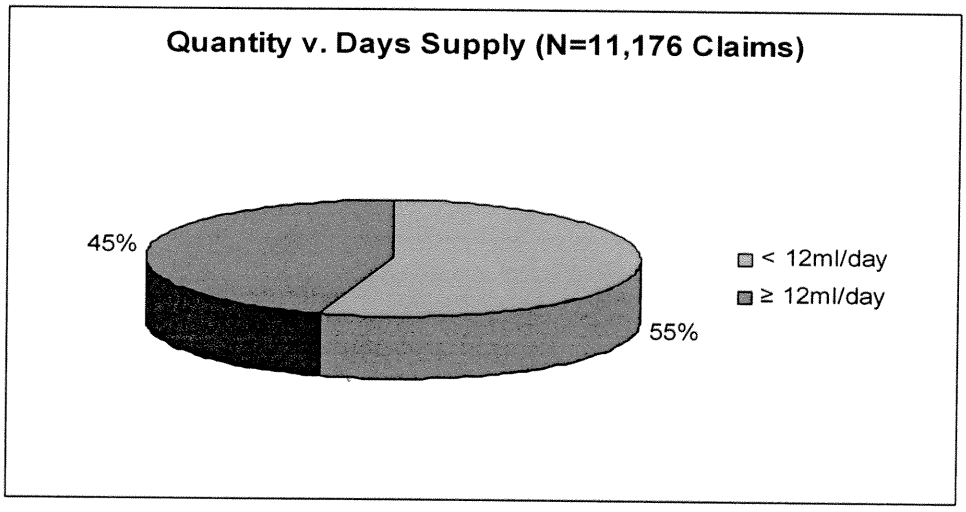


AGE GROUP	TOTAL PAID	TOTAL CLAIMS	COST PER CLAIM
0-5 years	$749,045.72	6,229	$120.25
6-18 years	$300,322.81	2,548	$117.87
19-34 years	$27,641.14	225	$122.85
35-49 years	$24,332.73	176	$138.25
50-64 years	$74,474.59	425	$175.23
65 years and over	$182,066.74	1,573	$115.74
Total	**$1,357,883.73**	**11,176**	**$121.50**

Looking at the claims for quantity dispensed versus days supply, sixty-six percent (66%) of the claims were for greater than 9ml/day (tid dosing = 9ml/day).



Forty-five percent (45%) of the claims were for 12ml/day or greater (qid dosing = 12ml/day).



Utilization Comparison with Albuterol Nebs

Dosing

Racemic albuterol is approved by the FDA for patients 2 years of age and older. Clinical practice and articles in the literature site use in neonatal to adult patients.

Albuterol Nebulization Dosage – Maintenance Therapy[4]				
Age	**Dose**	**0.083% Solution (ml/kg)**	**0.5% Solution (ml/kg)**	**Frequency**
< 12 years	0.15-0.25mg/kg (minimum: 1.25mg; Maximum: 5mg)	0.06-0.3 (minimum: 1.5ml; maximum: 6ml)	0.01-0.05 (minimum: 0.25ml; maximum: 1ml)	Every 4-6 hours
≥ 12 years	1.25-5mg		0.25-1ml	Every 4-6 hours

Appendix A-2 of the NAEPP Guidelines[1] lists the dosing for albuterol used for "quick relief" for children under 12 years as 0.05mg/kg (min 1.25mg, max 2.5mg) in 3ml of saline every 4-6 hours. Dosing for those 12 years of age and up is 1.25mg-5mg in 3ml of saline every 4-8 hours. NAEPP dosing for the treatment of exacerbations in the Emergency Department or Hospital is much more aggressive since the patient is continually monitored for adverse effects.

Utilization

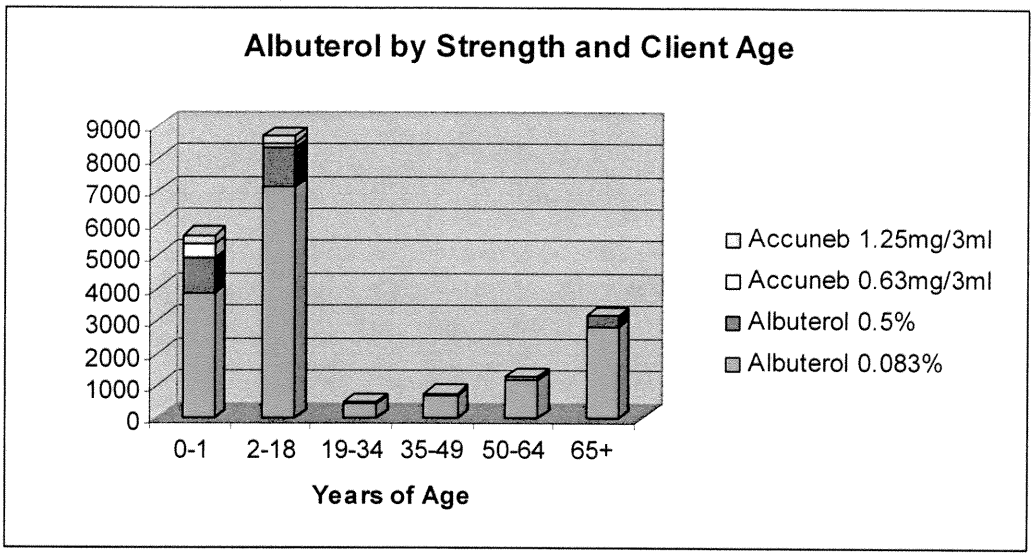
For the period of June 2003 to May 2004 a total of 20,130 clients received albuterol through the Medicaid fee-for-service program.

Drug	Claims	Total Units	Total Days	Total Cost	Total Clients	Per Diem
Albuterol 0.083% Neb	29,529	5,413,403	477,330	$502,165.66	16,067	$1.05
Albuterol 0.5% Neb	6,672	212,065	114,595	$65,937.04	3,595	$0.58
Accuneb 0.63mg/3ml	1,007	153,100	15,282	$77,999.58	664	$5.10
Accuneb 1.25mg/3ml	1,081	161,389	15,358	$81,549.73	723	$5.31
Totals	**38,289**	**5,939,957**	**622,565**	**$727,652.01**	**20,130***	**$1.17**

*Total number of non-duplicated clients

Total Cost 12 month period	**$727,652.01**	- 7.9%
Total Cost Previous 12 months	$789,725.17	
Total Claims 12 month period	**38,289**	**+ 17.6%**
Total Claims Previous 12 months	32,571	
Total Clients 12 month period	**20,130**	**+ 27.7%**
Total Claims Previous 12 months	15,763	
Per Diem 12 month period	**$1.17**	- 20.4%
Per Diem Previous 12 months	$1.47	

Claims were reviewed to determine the number of clients by age and drug strength. As you can see from the chart below, twenty-eight percent (28%) of the albuterol use is in clients under the approved age of 2 years.



AGE GROUP	TOTAL PAID	TOTAL CLAIMS	COST PER CLAIM
0-1 years	$197,361.99	8,647	$22.82
2-18 years	$270,445.77	15,214	$17.78
19-34 years	$20,370.20	1,153	$17.67
35-49 years	$34,122.51	1,762	$19.37
50-64 years	$72,815.77	3,529	$20.63
65 years and over	$132,536.07	7,984	$16.60
Total	**$727,652.01**	**38,289**	**$19.00**

Recommendations

Due to the evolving issue and body of literature discussing the physiological and clinical effects of S-albuterol, racemic albuterol, and levalbuterol, the College of Pharmacy has several suggested recommendations for the Board to consider. These recommendations have been drafted with the goal of encouraging clinical guideline adherence while allowing appropriate medication access.

1. Decrease the quantity limit on levalbuterol to 180ml/30day supply.
    a. Those clients needing quantities in excess of this amount could petition for an override.
    b. Clinical exceptions could be made for clients with COPD.
    c. The prescriber should explain why client is unable to use a long acting beta agonist and/or ICS therapy for long-term control per NAEPP guidelines.

   d. This should allow for acute exacerbations or pneumonias to have access for short term therapy without restriction.
2. Have a soft PA for levalbuterol.
   a. Allow for 90 days of therapy prior to the need to submit a petition for PA.
   b. Those clients still requiring medication after 90 days would submit a petition.
   c. The prescriber should explain why the client is unable to use a long acting beta agonist and/or ICS therapy for long-term control per NAEPP guidelines.
   d. Clinical exceptions can be made for clients with COPD.
   e. This would allow for acute exacerbations or pneumonias to have access for short term therapy without restriction (within the current quantity limits).
3. Have a hard PA for levalbuterol.
   a. A clinical exception can be made for those clients with COPD.
   b. The prescriber should explain why the client is unable to use a long acting beta agonist and/or ICS therapy for long-term control per NAEPP guidelines.
4. Consider enforcing age limitation per FDA approval on levalbuterol, currently 6 years of age and up OR consider age limitation for levalbuterol based upon clinical trials in literature of 2 years and up.
5. Consider restricting use of Xopenex® 1.25mg/3ml strength to clients 6 years of age and up.

References

1. Executive Summary of the National Asthma Education and Prevention Program (NAEPP). Expert Panel Report: Guidelines for the Diagnosis and Management of Asthma – Update on Selected Topics 2002. Bethesda, MD: National Institutes of Health; June 2002. NIH Publication 02-5075.

2. Global Initiative for Chronic Obstructive Lung Disease (GOLD), World Health Organization (WHO), National Heart, Lung and Blood Institute (NHLBI). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease – Update 2003. Bethesda (MD): Global Initiative for Chronic Obstructive Lung Disease, World Health Organization, National Heart, Lung and Blood Institute; 2003.

3. Product Information: Xopenex® (levalbuterol) Inhalation Solution, 0.31mg, 0.63mg, 1.25mg. Sepracor Inc, Marlborough, MA; (1/2002).

4. Guidelines for the Diagnosis and Management of Asthma. NAEPP Expert Panel Report 2," July 1997, www.nhlbi.nih.gov/guidelines/asthma/asthgdln.pdf.

Stepwise Approach for Managing Infants and Young Children (5 Years of Age and Younger) With Acute or Chronic Asthma

Classify Severity: Clinical Features Before Treatment or Adequate Control	Symptoms/Day Symptoms/Night	Medications Required To Maintain Long-Term Control Daily Medications
Step 4 Severe Persistent	Continual Frequent	■ Preferred treatment: – High-dose inhaled corticosteroids AND – Long-acting inhaled beta$_2$-agonists AND, if needed, – Corticosteroid tablets or syrup long term (2 mg/kg/day, generally do not exceed 60 mg per day). (Make repeat attempts to reduce systemic corticosteroids and maintain control with high-dose inhaled corticosteroids.)
Step 3 Moderate Persistent	Daily > 1 night/week	■ Preferred treatments: – Low-dose inhaled corticosteroids and long-acting inhaled beta$_2$-agonists OR – Medium-dose inhaled corticosteroids. ■ Alternative treatment: – Low-dose inhaled corticosteroids and either leukotriene receptor antagonist or theophylline. If needed (particularly in patients with recurring severe exacerbations): ■ Preferred treatment: – Medium-dose inhaled corticosteroids and long-acting beta$_2$-agonists. ■ Alternative treatment: – Medium-dose inhaled corticosteroids and either leukotriene receptor antagonist or theophylline.
Step 2 Mild Persistent	> 2/week but < 1x/day > 2 nights/month	■ Preferred treatment: – Low-dose inhaled corticosteroid (with nebulizer or MDI with holding chamber with or without face mask or DPI). ■ Alternative treatment (listed alphabetically): – Cromolyn (nebulizer is preferred or MDI with holding chamber) OR leukotriene receptor antagonist.
Step 1 Mild Intermittent	≤ 2 days/week ≤ 2 nights/month	■ No daily medication needed.

Quick Relief
All Patients

- Bronchodilator as needed for symptoms. Intensity of treatment will depend upon severity of exacerbation.
  - Preferred treatment: **Short-acting inhaled beta$_2$-agonists** by nebulizer or face mask and space/holding chamber
  - Alternative treatment: Oral beta$_2$-agonist
- With viral respiratory infection
  - Bronchodilator q 4–6 hours up to 24 hours (longer with physician consult); in general, repeat no more than once every 6 weeks
  - Consider systemic corticosteroid if exacerbation is severe or patient has history of previous severe exacerbations
- Use of short-acting beta$_2$-agonists >2 times a week in intermittent asthma (daily, or increasing use in persistent asthma) may indicate the need to initiate (increase) long-term-control therapy.

Step down
Review treatment every 1 to 6 months; a gradual stepwise reduction in treatment may be possible.

Step up
If control is not maintained, consider step up. First, review patient medication technique, adherence, and environmental control.

Goals of Therapy: Asthma Control

- Minimal or no chronic symptoms day or night
- Minimal or no exacerbations
- No limitations on activities; no school/parent's work missed
- Minimal use of short-acting inhaled beta$_2$-agonist
- Minimal or no adverse effects from medications

Note

- The stepwise approach is intended to assist, not replace, the clinical decisionmaking required to meet individual patient needs.
- Classify severity: assign patient to most severe step in which any feature occurs.
- There are very few studies on asthma therapy for infants.
- Gain control as quickly as possible (a course of short systemic corticosteroids may be required); then step down to the least medication necessary to maintain control.
- Minimize use of short-acting inhaled beta$_2$-agonists. Overreliance on short-acting inhaled beta$_2$-agonists (e.g., use of approximately one canister a month even if not using it every day) indicates inadequate control of asthma and the need to initiate or intensify long-term-control therapy.
- Provide parent education on asthma management and controlling environmental factors that make asthma worse (e.g., allergies and irritants).
- Consultation with an asthma specialist is recommended for patients with moderate or severe persistent asthma. Consider consultation for patients with mild persistent asthma.

Stepwise Approach for Managing Asthma in Adults and Children Older Than 5 Years of Age: Treatment

Classify Severity: Clinical Features Before Treatment or Adequate Control	Symptoms/Day Symptoms/Night	PEF or FEV_1 PEF Variability	Medications Required To Maintain Long-Term Control Daily Medications
Step 4 Severe Persistent	Continual Frequent	≤ 60% > 30%	■ Preferred treatment: – **High-dose inhaled corticosteroids** AND – **Long-acting inhaled $beta_2$-agonists** AND, if needed, – Corticosteroid tablets or syrup long term (2 mg/kg/day, generally do not exceed 60 mg per day). (Make repeat attempts to reduce systemic corticosteroids and maintain control with high-dose inhaled corticosteroids.)
Step 3 Moderate Persistent	Daily > 1 night/week	> 60% – < 80% > 30%	■ Preferred treatment: – **Low-to-medium dose inhaled corticosteroids and long-acting inhaled $beta_2$-agonists.** ■ Alternative treatment (listed alphabetically): – Increase inhaled corticosteroids within medium-dose range OR – Low-to-medium dose inhaled corticosteroids and either leukotriene modifier or theophylline. If needed (particularly in patients with recurring severe exacerbations): ■ Preferred treatment: – **Increase inhaled corticosteroids within medium-dose range and add long-acting inhaled $beta_2$-agonists.** ■ Alternative treatment (listed alphabetically): – Increase inhaled corticosteroids within medium-dose range and add either leukotriene modifier or theophylline.
Step 2 Mild Persistent	> 2/week but < 1x/day > 2 nights/month	≥ 80% 20–30%	■ Preferred treatment: – **Low-dose inhaled corticosteroids.** ■ Alternative treatment (listed alphabetically): cromolyn, leukotriene modifier, nedocromil, OR sustained-release theophylline to serum concentration of 5–15 mcg/mL.
Step 1 Mild Intermittent	≤ 2 days/week ≤ 2 nights/month	≥ 80% < 20%	■ No daily medication needed. ■ Severe exacerbations may occur, separated by long periods of normal lung function and no symptoms. A course of systemic corticosteroids is recommended.

Quick Relief
All Patients

- Short-acting bronchodilator: 2–4 puffs **short-acting inhaled $beta_2$-agonists** as needed for symptoms.
- Intensity of treatment will depend on severity of exacerbation; up to 3 treatments at 20-minute intervals or a single nebulizer treatment as needed. Course of systemic corticosteroids may be needed.
- Use of short-acting $beta_2$-agonists >2 times a week in intermittent asthma (daily, or increasing use in persistent asthma) may indicate the need to initiate (increase) long-term-control therapy.

Step down
Review treatment every 1 to 6 months; a gradual stepwise reduction in treatment may be possible.

Step up
If control is not maintained, consider step up. First, review patient medication technique, adherence, and environmental control.

Goals of Therapy: Asthma Control

- Minimal or no chronic symptoms day or night
- Minimal or no exacerbations
- No limitations on activities; no school/work missed
- Maintain (near) normal pulmonary function
- Minimal use of short-acting inhaled $beta_2$-agonist
- Minimal or no adverse effects from medications

Note

- The stepwise approach is meant to assist, not replace, the clinical decisionmaking required to meet individual patient needs.
- Classify severity: assign patient to most severe step in which any feature occurs (PEF is % of personal best; FEV_1 is % predicted).
- Gain control as quickly as possible (consider a short course of systemic corticosteroids); then step down to the least medication necessary to maintain control.
- Minimize use of short-acting inhaled $beta_2$-agonists. Overreliance on short-acting inhaled $beta_2$-agonists (e.g., use of approximately one canister a month even if not using it every day) indicates inadequate control of asthma and the need to initiate or intensify long-term-control therapy.
- Provide education on self-management and controlling environmental factors that make asthma worse (e.g., allergens and irritants).
- Refer to an asthma specialist if there are difficulties controlling asthma or if step 4 care is required. Referral may be considered if step 3 care is required.

APPENDIX E

Hepatitis C Drugs
Oklahoma Medicaid Utilization
September 14, 2004

Introduction

Hepatitis C is a mostly asymptomatic acute and chronic liver disease, caused by the hepatitis C virus (HCV), which can progress from acute inflammation to cirrhosis, end-stage liver failure, and possible hepatocellular carcinoma over the course of several decades. However, up to 45% of those infected with HCV will clear the virus spontaneously and not require treatment. Because of the mode of transmission, HCV is often a co-infection with HIV; approximately 10% of the 2.7 million people believed to have chronic hepatitis C also have HIV.

The HCV has six major genotypes. Establishing which genotype is causing the infection can be useful in predicting response to treatment and to determine the length of treatment. Infected blood and blood products transmit the virus.

Population at risk (per CDC recommendations)

- Persons who have used illicit drugs in the recent or remote past, even once
- Hemophiliacs who received blood products before 1987
- Persons who received a blood transfusion or organ transplant before July 1992.
- Persons with unexplained elevation of aminotransferase levels (ALT/AST)
- Persons with HIV infection
- Persons who have ever been on hemodialysis
- Children born to HCV-infected mothers
- Health care, emergency medical and public safety workers after a needle stick or mucosal exposure to HCF-positive blood
- Current sexual partners of HCF infected.

Available FDA Approved Treatment

Drug	How Supplied	Indications
Peginterferon alfa-2a (Pegasys®)	Injection, solution: 180 mcg/mL (1.2 mL) Injection, solution [prefilled syringe]: 180 mcg/mL (0.5 mL) packaged with needles and alcohol swabs]	*Adults*: Treatment of chronic hepatitis C, alone or in combination with ribavirin, in patients with compensated liver disease.
Peginterferon alfa-2b (Peg-Intron®)	Injection, powder for reconstitution [prefilled syringe] (Redipen™): 50 mcg, 80 mcg, 120 mcg, 150 mcg [packaged with alcohol swabs and needle for injection] Injection, powder for reconstitution [vial]: 50 mcg, 80 mcg, 120 mcg, 150 mcg [packaged with SWFI, alcohol swabs, and syringes]	*Adults*: Treatment of chronic hepatitis C (as monotherapy or in combination with ribavirin) in patients who have never received interferon alpha and have compensated liver disease
Ribavirin (Copegus®, Rebetol®)	Capsule (Rebetol®, Ribasphere™): 200 mg Powder for aerosol (Virazole®): 6 g Solution, oral (Rebetol®): 40 mg/mL (100 mL) [contains sodium benzoate; bubblegum flavor] Tablet (Copegus®): 200 mg	*Children*: Treatment of patients with respiratory syncytial virus (RSV) infections Adults: In combination with interferon (pegylated or nonpegylated) injection for the treatment of chronic hepatitis C in patients with compensated liver disease who have relapsed after alpha interferon therapy or were previously untreated with alpha interferons

Drug	How Supplied	Indications
Interferon Alfa-2b and Ribavirin (Rebetron®)	Injection, sol'n: Interferon alfa-2b (Intron® A): 3 mU/0.5 mL (0.5 mL) [6 vials (mU/vial), 6 syringes and alcohol swabs] plus Capsules: Ribavirin (Rebetol®): 200 mg Injection, sol'n: Interferon alfa-2b (Intron® A): 3 Mu/0.5 mL (3.8 mL) [1 multidose vial (18 mU/vial), 6 syringes and alcohol swabs] plus Capsules: Ribavirin (Rebetol®): 200 mg Injection, sol'n: Interferon alfa-2b (Intron® A): 3 Mu/0.2 mL (1.5 mL) [1 multidose pen (18 mU/pen), 6 needles and alcohol swabs] plus Capsules: Ribavirin (Rebetol®): 200 mg	Adults & Children (*≥3 years):* Combination therapy for the treatment of chronic hepatitis C in patients with compensated liver disease previously untreated with alpha interferon or who have relapsed after alpha interferon therapy
Interferon alfa 2b (Intron-A®)	Injection, powder for reconstitution: 3 mU; 5 mU; 10 mU; 18 mU; 25 mU; 50 mU Injection, solution [multidose prefilled pen]: 3 mU /0.2 mL (1.5 mL) [6 doses; 18 mU];5 mU /0.2 mL (1.5 mL) [6 doses; mU]; 10 mU/0.2 mL (1.5 mL) [6 doses; 60 mU Injection, solution [multidose vial]: 6 mU/mL (3 mL); 10 mU/mL (2.5 mL) Injection,solution [single-dose vial]: 3 mU/0.5 mL (0.5 mL); 5 mU/0.5 mL (0.5 mL); 10 mU/ mL (1 mL)	*Children 1-17 years*: Chronic hepatitis B *Adults*: Hairy cell leukemia; Lymphoma (follicular); Malignant melanoma; AIDS-related Kaposi's sarcoma; Chronic hepatitis B; Chronic hepatitis C; Condyloma acuminate.
Interferon alfa-2a (Roferon-A®)	Injection, solution [multidose vial]: 6 mU/mL (3 mL); Injection, solution, [single-dose prefilled syringe; SQ use only]: 3 mU/0.5 mL (0.5 mL); 6 mU/0.5 mL (0.5 mL); 9 mU/0.5 mL (0.5 mL) Injection, solution [single-dose vial]: 36 mU/mL (1 mL)	*Children*: Chronic myelogenous leukemia (CML): *Adults*: Hairy cell leukemia; Chronic myelogenous leukemia (CML); AIDS-related Kaposi's sarcoma; Hepatitis C
Interferon alfacon-1 (Infergen®	Injection, solution: 30 mcg/mL (0.3 mL, 0.5 mL) [prefilled syringe or single-dose vial]	*Adults(≥18 yrs)*: Treatment of chronic hepatitis C virus (HCV) infection in patients with compensated liver disease and anti-HCV serum antibodies or HCV RNA.

Recommended Hepatitis C Dosing Regimens

Genotype	Weight	Drug/Dose	Duration
1,4	≤75 kg	Pegasys 180 mcg SQ/wk + Copegus 400 mg po qam & 600 mg po qpm	48 weeks
	>75 mg	Pegasys 180 mcg SQ/wk + Copegus 600 mg BID	
2,3		Pegasys 180 mcg SQ/wk + Copegus 400 mg BID	24 weeks
		Peg-Intron 1.5 mcg/kg SQ/wk + Rebetol 400 mg po BID (Weight ranges for doses are established for Peg-Intron monotherapy and combination therapy with Rebetol)	24 weeks
		Pegasys 180 mcg SQ once weekly	48 weeks
		Peg-Intron 1.0 mcg/kg SQ once weekly	1 year
1	25-61 kg	Rebetron: *Children ≥3* years: Combination therapy: Intron-A®: 3 mU/m^2 SQ 3 times/week Rebetol®: Oral: Capsule/solution: 15 mg/kg/day in 2 divided	48 weeks

Genotype	Weight	Drug/Dose	Duration
		doses. **Note:** Oral solution should be used in children 3-5 years of age, children ≤25 kg, or those unable to swallow capsules (>61 kg, use adult dosing)	
2, 3	25-61 kg	See above	24 weeks
	≤75 kg	Rebetron – Intron-A 3 mU SQ TIW + Rebetol 1000 mg po QD	Relapse after alpha interferon alone: 24 weeks. Previously untreated: 24-48 weeks (individualized based on response, tolerance, and baseline characteristics) Consider discontinuing therapy in any patient not achieving HCV-RNA below the limit of assay detection by 24 weeks
	>75 mg	Rebetron – Intron-A 3 mU SQ TIW + Rebetol 1200 mg po QD (in two divided doses	
		Roferon-A® 3 mU SQ TIW	12 months
		Intron A® 3 mU SQ TIW	16 wks, then 18-24 mos if ALT normalized
		Infergen 9 mcg SQ TIW	24 weeks
		Infergen 15 mcg SQ TIW in nonresponders	6 months

Treatment widely accepted for patients who:

- Are ≥ 18 years old
- Have abnormal ALT values
- Have a liver biopsy with chronic hepatitis with significant fibrosis (more-than-portal)
- Have compensated liver disease (T-bili <1.5 g/dl, INR <1.5, Albumin >3.4 g/dl, platelets >75,000 mm^3), without evidence of hepatic encephalopathy or ascites
- Have acceptable CBC/Chemistry: Hgb >13 g/dl (♂), >12 g/dl (♀), neutrophil count >1.5K/ mm^3, serum creatinine <1.5 mg/dl mm^3
- Have been treated previously for HCV
- If being treated for depression, are well controlled
- Are willing to be treated and to conform to requirements

Treatment individualized for patients who:

- Have persistently normal ALT values
- Have failed prior therapy with interferon +/- ribavirin, or peginterferon alone
- Are current users of illicit drugs or alcohol, but who are willing to undergo rehab program
- Have liver biopsy evidence of either no or only mild fibrosis
- Have acute Hepatitis C
- Are co-infected with HIV
- Are <18 years old
- Have chronic renal disease (on or not on hemodialysis)
- Have decompensated cirrhosis
- Are a liver transplantation recipient

Treatment contraindicated for patients who:

- Have major, uncontrolled depressive illness
- Are a kidney, renal, or lung transplant recipient
- Have autoimmune hepatitis or other condition know to be exacerbated by interferon and ribavirin
- Have untreated hyperthyroidism
- Are pregnant or unwilling/unable to comply with adequate contraception
- Have severe concurrent disease such as severe hypertension, heart failure, significant coronary artery disease, poorly controlled diabetes, obstructive pulmonary disease

- Are < 3 years old
- Have know hypersensitivity to drugs used to treat HCV

Oklahoma Medicaid Utilization FY 2004 (July 2003-June 2004)

General Usage:

Total paid: FY 2004	**$2,513,006.13**	**58.5% ↑**
Total paid FY 2003	*$1,585,224.41*	
Total # of clients: FY 2004	**227clients**	**24.7% ↑**
Total # of clients: FY 2003	*182 clients*	
Total # of Hepatitis C drug claims: FY 2004	**1,757 claims**	**42.2% ↑**
Total # of Hepatitis C drug claims: FY 2003	*1,236 claims*	
Per Diem: FY 2004	**$49.92**	**10.8% ↑**
Per Diem: FY 2003	*$45.05*	

Pharmacy Claims

Product	# of Claims	Total Units	Total Days	Total Cost	Total Clients*	Per Diem
Pegasys® Inj 180mcg/ml	112	454	3144	$144,119.20	28	$45.84
Pegasys® Kit 180mcg/ml	282	594	8620	$549,123.44	73	$63.70
Peg-Intron® Kit 50 mcg	47	261	1300	$62,912.51	8	$48.39
Peg-Intron® Kit 80 mcg	92	384	2539	$127,018.58	24	$50.03
Peg-Intron® Kit 120 mcg	199	805	5215	$281,762.59	48	$54.03
Peg-Intron® Kit 150 mcg	193	1148	5743	$294,230.91	45	$51.23
Rebetol® 200 mg cap	477	74677	13843	$722,626.47	127	$52.20
Copegus® 200 mg tab	245	39523	7235	$223,516.64	64	$30.89
Rebetron® Kit 1200 mg caps	11	18	228	$14,101.56	3	$61.85
Roferon-A® 3mU/0.5 ml	6	90	204	$3,042.30	1	$14.91
Intron-A® Inj 18 mU	29	348	681	$30,600.79	3	$44.94
Intron-A® Inj 25 mU	2	20	28	$2,866.98	1	$102.39
Intron-A® Inj 3 mU pen	25	244	726	$18,418.22	6	$25.37
Intron-A® Inj 5 mU pen	9	21	278	$6,163.35	1	$22.17
Intron-A® Inj 10 mU pen	4	80	156	$12,354.84	2	$79.20
Intron-A® Inj 3 mU	1	6	9	$227.23	1	$25.25
Intron-A® Inj 5 mU	1	15	35	$939.88	1	$26.85
Intron-A® Inj 10 mU	1	12	30	$1,793.44	1	$59.78
Intron-A® Inj 18 mU	1	12	30	$3,226.35	1	$107.55
Intron-A® Kit 10 mU/mL	6	66	154	$9,762.91	1	$63.40
Infergen® Inj 15mcg/0.5ml	4	33	146	$4,196.64	2	$28.74
Totals	**1,757**	**118,812**	**50,344**	**$2,513,006.13**	**227**	

*Unduplicated clients **Units include tablets, capsules, kits and milliliters.

Clinic Claims - *Interferon alfa 2b (Intron-A®)

Drug	Total Clients	Total Claims	Total Units	Total Cost
FY 2004	6	133	2190	$31,098.00
FY 2003	*10*	*119*	*1980*	*$28,116.00*

**Intron-A was the only interferon product used in clinic setting. Information for pegylated products could not be retrieved as they do not have an assigned HCPCS code.*

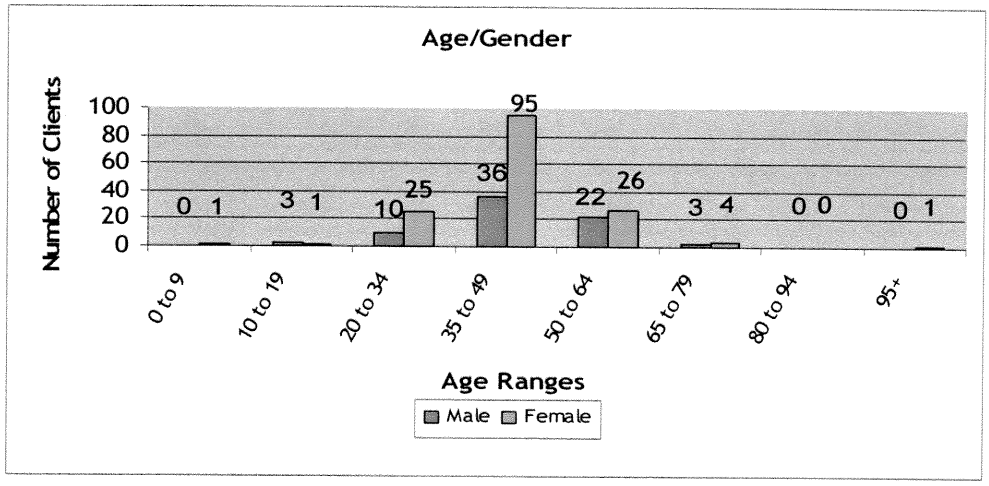
Diagnosis Information

Of the 227 clients who received treatment for Hepatitis C through a pharmacy, 189 had a specific diagnosis of hepatitis C, either acute or chronic. 211 of these clients had an ICD-9 code for liver disease of some type (except alcohol related). Four clients had a co-infection with HIV.

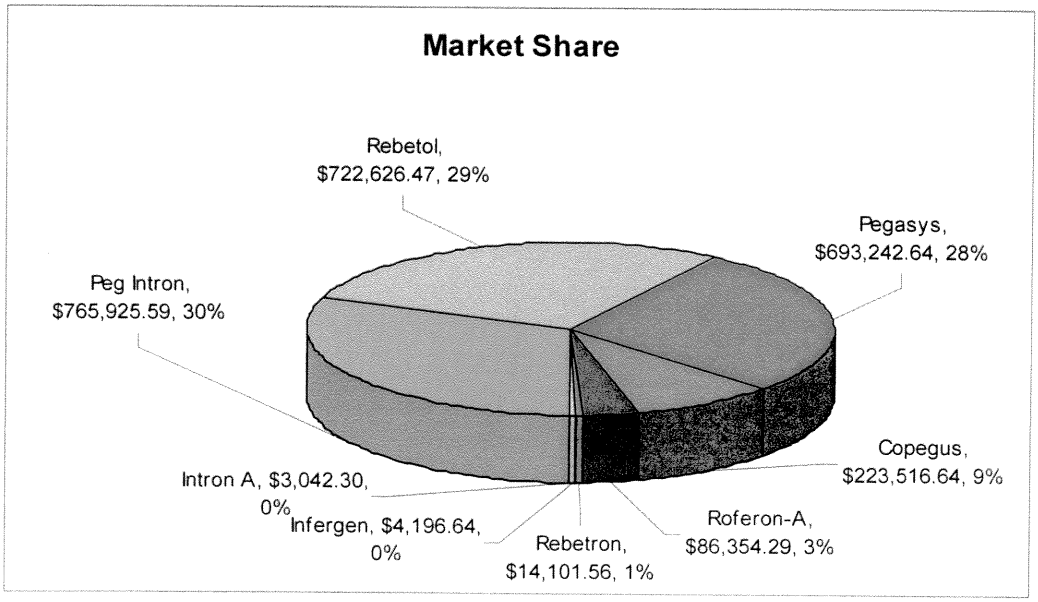
Of the14 pharmacy clients who were treated with a nonpegylated interferon product, four had a diagnosis of acute hepatitis C, three had a diagnosis of hepatitis B, five had a cancer diagnosis, and two could not be determined.

All of the clients who received a nonpegylated interferon product (Intron-A was the only one used) in the clinic setting were treated for cancer. Pegylated products do not have a J-code assignment at this time, so their use in the clinic setting could not be determined.

Demographic Information



In looking at market share, it must be remembered that Rebetrol is only used in combination with Peg-Intron, as is Copegus used with Pegasys. But Peg-Intron and Pegasys can be used as monotherapy.



Conclusion

Pegylated alfa interferon (2a and 2b), alone or with ribavirin, is the standard treatment for Chronic Hepatitis C. While nonpegylated alfa interferon still has the FDA approved indication for Hepatitis C, it is primarily used in chemotherapy protocols.

Recommendations

The College of Pharmacy recommends continued monitoring of these products. The trend is toward increased chronic hepatitis C infection. Future increased use of pegylated interferon could be possible with recent studies for cancer treatment.

APPENDIX F

Drug Utilization Review of Restasis®

Oklahoma Medicaid
Fiscal Year 2004

Introduction[1]

Keratoconjunctivitis sicca (also known as Chronic Dry Eye Disease) is a condition that can result from the eyes' reduced ability to produce tears and may lead to chronic irritation and destruction of corneal and bulbar conjunctival epithelium. The exact etiology is unknown, but inflammation is believed to be an important causative factor. Keratoconjunctivitis sicca (KCS) is often an ocular manifestation of such diseases as viral Hepatitis C infections, and automimmune disorders such as Sjögren's Syndrome, Systemic Lupus Erythmatosus, and Lichen planus in which the body's normal body inflammatory levels are elevated. Among the current available treatments are eye lubricants, topical corticosteroids, and topical cyclosporine emulsion (Restasis®).

Indication & Usage[2]:

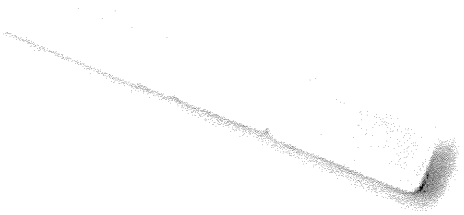
Restasis® is thought to act as a partial immunomodulator, but the exact mechanism us unknown. It is FDA indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with KCS.

Restasis® ophthalmic emulsion is packaged in sealed trays containing 32 single use vials. The vial should be inverted several times before use and one drop should be instilled in each each eye twice daily (approximately 12 hours apart.)

RESTASIS® is packaged in single-usage (one drop per eye) disposable droppers.

Restasis® is contraindicated in patients with active ocular infections and in patients with known or suspected hypersensitivity to any of the ingredients in the formulation.

The most common adverse effects are ocular burning (17%). Other events reported in 1% to 5% of patients included conjunctival hyperemia, discharge, epiphora, eye pain, foreign body sensation, pruritus, stinging, and visual disturbance (most often blurring).



Restasis Utilization

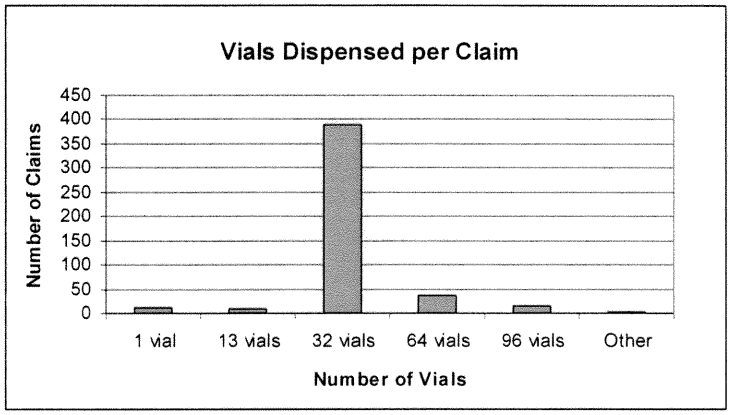
For the period of July 2003 through June 2004, a total of 167 clients received Restasis® through the Medicaid fee-for-service program.

Utilization Totals for Fiscal Year 2004

Clients	*Claims*	*Cost*	*Claim/Client*	*Quant/Claim*	*Perdiem*
167	*468*	*$ 44,082.37*	*2.80*	*37 vials*	*$ 5.16*

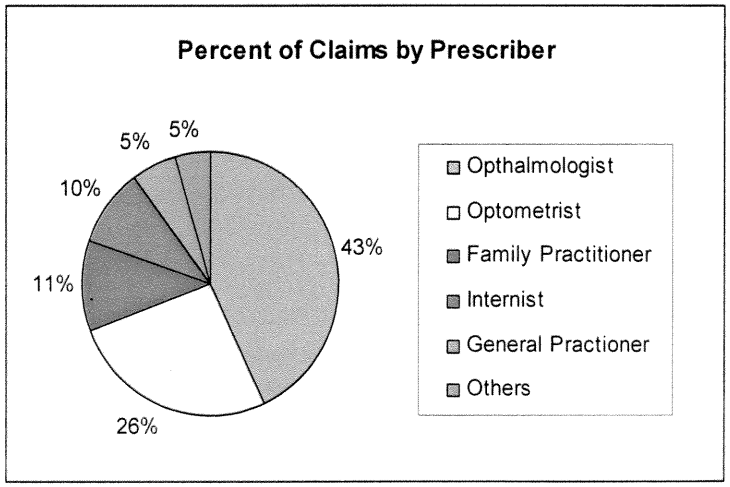
Vials Dispensed per Claim

The package insert states the entire contents of the tray (32 vials) must be dispensed as one unit. The claims data show that the trays are opened and partially dispensed in about 5.5% (26/468) of the claims, all of which were dispensed by closed door pharmacies.

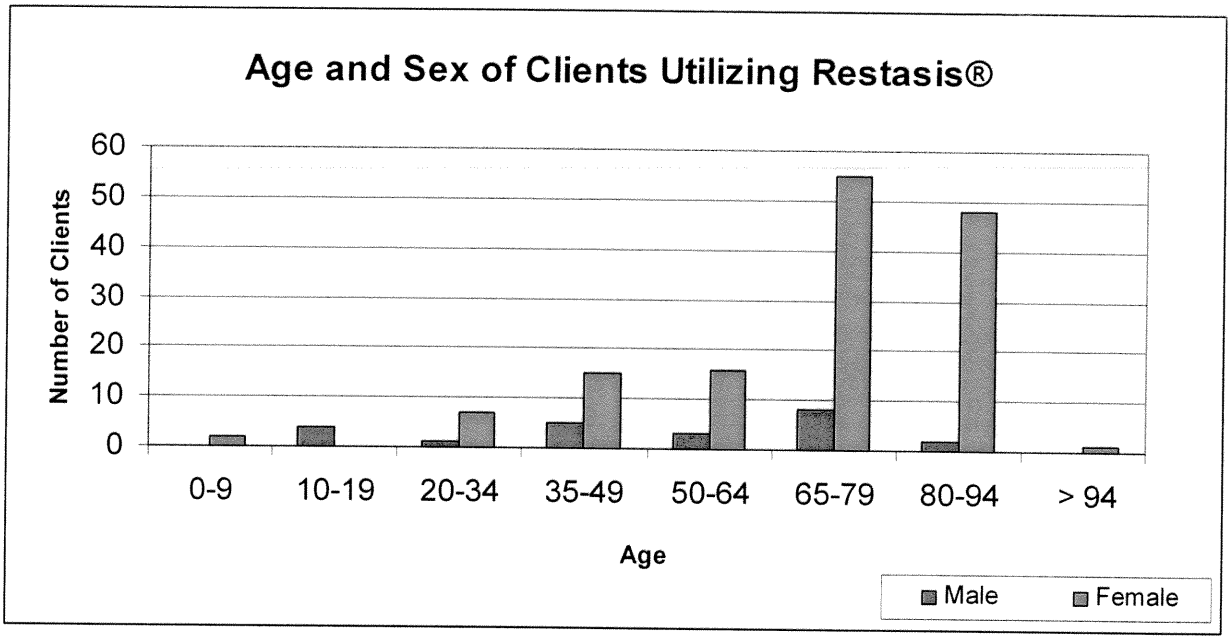


Percent of Claims by Prescriber

43% of the claims were prescribed by an Opthalmologist, which is consistent with the disease state involved. Approximately 4.3% (20/468) of the claims were prescribed by "Other" prescribers, such as: Psychiatrist, Thoracic Surgeon, General Surgeon, and General Pediatrician.



Client Demographics



The vast majority of the clients were elderly females from 65 to 94 years old. Approximately 19% (31/167) of the clients were in nursing homes. 84% (26/31) of the clients in the nursing homes were female.

Female gender has been reported to be a risk factor for developing KCS, particularly when associated with Sjögren's Syndrome. Sjögren's Syndrome is more predominant in females than males and has a late age of onset specifically around the perimenopausal period.

Recommendations

The College of Pharmacy recommends no further action at this time as the results of the drug utilization review suggests Restasis® is being prescribed and used appropriately. The college will continue to monitor the utilization of this medication.

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[1] Pflugfelder SC, Solomon, A, Stern ME. The diagnosis and management of dry eye: A twenty five year review. Journal of Cornea and External Disease. September 2000: Vol 19(5); 644-649.

[2] Allergan Pharmaceuticals. Package Literature Restasis®. February 2004.

APPENDIX G

Drug Utilization Review of Anti-Emetics

Oklahoma Medicaid

September 2004

Introduction

Nausea and vomiting is a common symptomatic manifestation of certain medical conditions or procedures, or can often occur as an adverse effect of certain medications. There is an array of medications that have been proven to have anti-emetic effects, among which are the antihistamines, benzamides, cannabinoids, phenothiazines, belladonna alkaloids such as scopolamine, 5-HT3 receptor antagonists, and most recently, the substance P antagonists. The first line anti-emetic of choice is dependent on the cause of the vomiting and the side effect profile of the medication.

Trends in Anti-Emetic Utilization

	Fiscal Year 2003	*Fiscal Year 2004*	*Percent Change*	
Total Claims	**12,417**	**9,574**	**Decreased**	**22.9 %**
Antidopaminergic	25	2	Decreased	92 %
Anticholinergic	10,451	6,286	Decreased	39.9 %
Cannabinoids	309	368	Increased	19.1 %
5-HT3 Receptor Antagonists	1,631	2,905	Increased	78.1 %
Substance P Antagonist	2	13	Increased	550 %
Total Cost	**$ 1,138,522.60**	**$ 1,880,120.80**	**Increased**	**65.1 %**
Antidopaminergic	$ 882.56	$ 29.90	Decreased	96.6 %
Anticholinergic	$ 124,322.67	$ 83,461.67	Decreased	32.9 %
Cannabinoids	$ 114,400.55	$ 136,318.12	Increased	19.2 %
5-HT3 Receptor Antagonists	$ 898,737.49	$ 1,654,003.09	Increased	84.0 %
Substance P Antagonist	$ 179.34	$ 6,308.26	Increased	3,417 %
Cost per Claim	**$ 91.68**	**$ 196.38**	**Increased**	**114 %**
Antidopaminergic	$ 35.30	$ 14.95	Decreased	57.6 %
Anticholinergic	$ 11.90	$ 13.28	Increased	11.6 %
Cannabinoids	$ 370.23	$ 370.43	Increased	0.00 %
5-HT3 Receptor Antagonists	$ 551.03	$ 569.36	Increased	3.33 %
Substance P Antagonist	$ 89.70	$ 485.25	Increased	440 %

5-HT3 Receptor Antagonists

The most expensive class of anti-emetics is the 5-HT3 receptor antagonists in regards to cost per claim. This class accounted for only 30% of the claims, yet incurred 88% of the cost. The following are the currently available 5-HT3 receptor antagonists and their FDA approved indications.

Medication		CINV*	RINV+	PONV@
Ondansetron[1]	(Zofran®)	Yes	Yes	Yes
Granisetron[2]	(Kytril®)	Yes	Yes	Yes
Dolasetron[3]	(Anzemet®)	Yes	No	Yes
Palonosetron[4]	(Aloxi®)	Yes	No	No

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

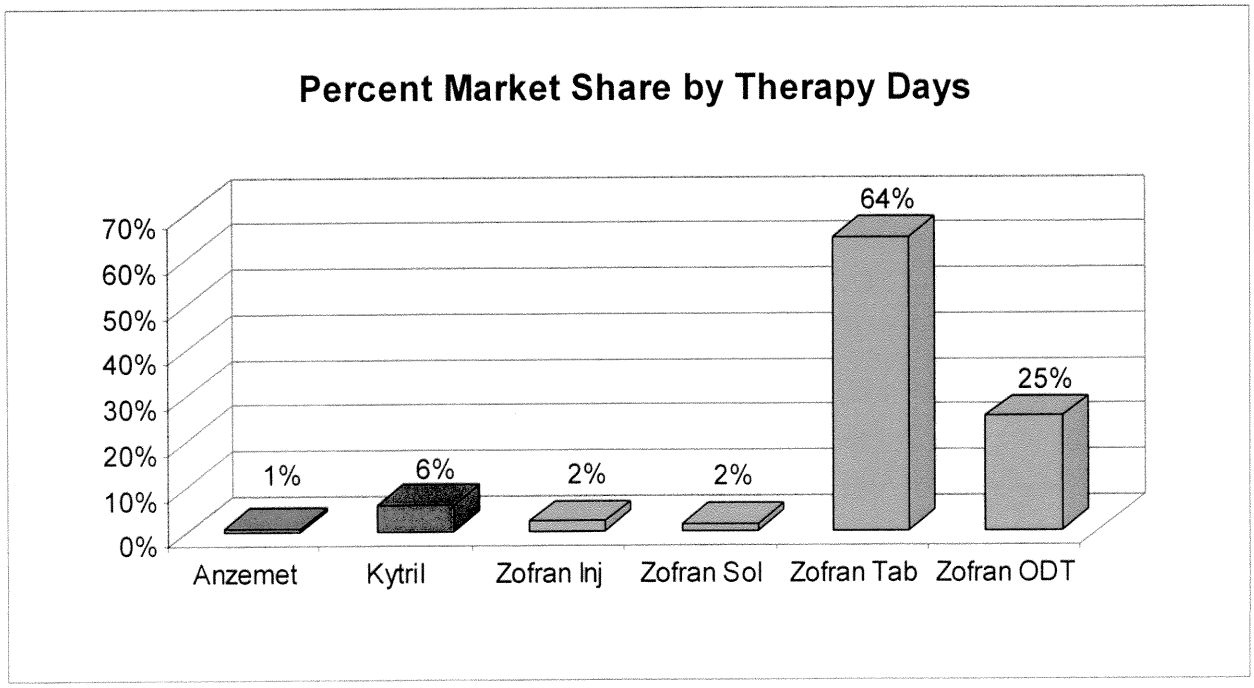
Utilization

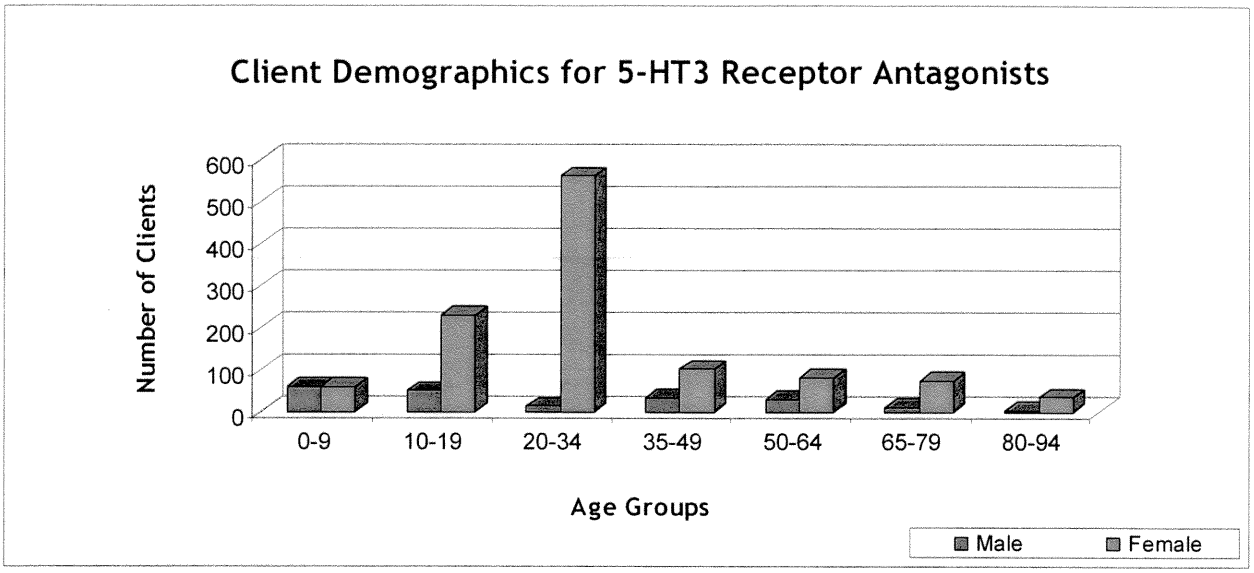
For the period of July 2003 through June 2004, a total of 1,346 clients received 5-HT3 receptor antagonists through the Medicaid fee-for-service program resulting in 2,905 claims and an incurred cost of $1,654,003.09. The details are as follows:

Drug*		Client	Claims	Cost	Cost/Claim	Claim/ Client	Days/ Claim	Units/ Day
ANZEMET®	TAB 50MG	2	2	$ 3,547.64	$ 1,773.82	1	10	3.5
ANZEMET®	TAB 100MG	15	23	$ 16,468.93	$ 716.04	2	7	1.4
KYTRIL®	TAB 1MG	47	98	$ 95,130.38	$ 970.72	2	13	1.8
KYTRIL®	INJ 1MG/ML	1	17	$ 3,677.91	$ 216.35	17	5	0.2
ZOFRAN®	INJ 2MG/ML	15	45	$ 61,254.67	$ 1,361.21	3	12	16.3
ZOFRAN®	SOL 4MG/5ML	15	29	$ 7,503.95	$ 258.76	2	13	5.4
ZOFRAN®	TAB 4MG	492	975	$ 481,363.16	$ 493.71	2	8	3.3
ZOFRAN®	TAB 8MG	358	747	$ 607,780.74	$ 813.63	2	10	2.8
ZOFRAN ODT®	TAB 4MG	283	493	$ 134,216.76	$ 272.24	2	5	2.9
ZOFRAN ODT®	TAB 8MG	254	476	$ 243,058.95	$ 510.63	2	7	2.6

* There were no Aloxi® claims within the researched timeframe.

Zofran® was the first of the 5-HT3 receptor antagonists to enter the market. It currently holds 93% of the market share among the 5-HT3 receptor antagonists. Zofran® oral tablets are the most commonly prescribed followed by the Zofran® orally disintegrating tablets.





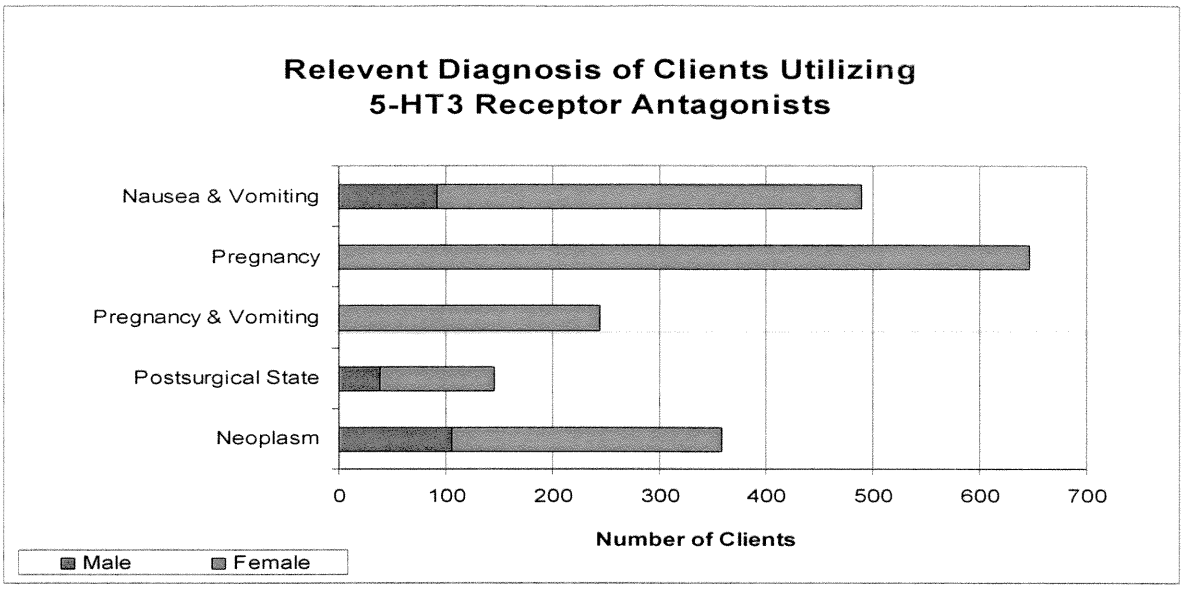
The trend of female clients being more prevalent over male clients is consistent with the general demographics of the Medicaid population. However, there is a sharp increase in female clients countered by the decrease in male clients in the 20-34 year old age group that is atypical and inconsistent with national cancer incidence rates.[5]

Apropriate Utilization of 5-HT3 Receptor Antagonists Acccording to Diagnosis

As mentioned above, 5-HT3 receptor antagonists are only FDA approved for nausea and vomiting related to cancer treatment therapies such as chemotherapy or radiation therapy. They are also approved for use in clients at risk for post operative nausea and vomiting. Due to the high cost of these medications many researchers as well as institutions have compiled concensus guidelines[6,7,8] to minimize the costs by effectively identifying risk factors for nausea and vomiting. Many clinics and hospitals have adopted these guidelines and currently have set protocols that reserve the 5-HT3 receptor antagonists only for clients with a high risk of nausea/vomiting. The risk is determined by the type of chemotherapy agent, area of radiation, type and duration of surgery, or patient specific factors.

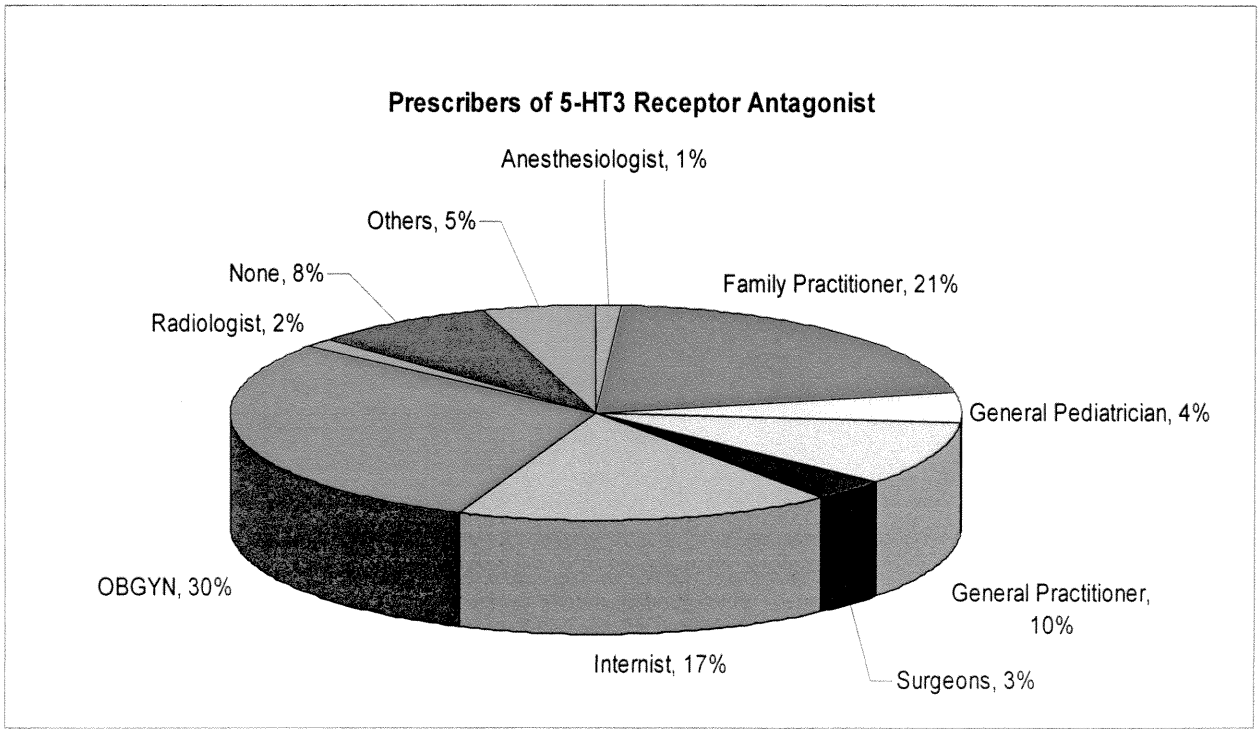
A diagnosis search was conducted for all Medical/hospital claims of clients who've received 5-HT3 receptor antagonist during fiscal yearl 2004. A total of 1,346 clients yielded 28,459 diagnoses. Among all the diagnoses several diagnostic categories of interested were filtered out and the results are as follows:

ICD-9 Codes	*Description*	*Male*	*Female*	*Total Clients*
140-239	Neoplasm/Cancer - all types	106	252	358
V42-45	Post Surgical State	38	107	145
643	Varying degrees of Vomiting during Pregnancy	0	244	244
v22	Pregnancy with no complications specified	0	647	647
787	Nausea & Vomiting	92	396	488



Prescribers of 5-HT3 Receptor Antagonists

The prescribers of the 5-HT3 receptor antagonists in the Oklahoma Medicaid population were also categorized. According to pharmacy claims during fiscal year 2004 the top prescribers of 5-HT3 receptor antagonists were obstetricians/gynecologists at 30% followed by family practitioners at 21%. Surgeons and radiologists only accounted for a total of 5% of the pharmacy claims.



Conclusion

The 5-HT3 receptor antagonists is an effective class of medication that can help improve the quatility of life for clients clients who are undergoing cancer treatment therapy or surgical procedures that are at high risk for nausea and vomiting. However, the data suggests that the 5-HT3 receptor antagonists may also be used inappropriately for nausea and vomiting associated with pregnancy.

5-HT3 receptor antagonists are not among the typical interventions used for nausea and vomiting in pregnancy. All currently available 5-HT3 receptor antagonists are classified as FDA Pregnancy Category B. Studies using Zofran® during pregnancy are limited, and did not demonstrated Zofran® to be superior to other antiemetics in hyperemesis gravidarum.[9]

Recommendations

The College of Pharmacy recommends that the DUR board consider prior authorization of the 5-HT3 receptor antagonists to ensure appropriate utilization.

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[1] GlaxoSmithKline Pharmaceuticals. Package literature Zofran®. May 2004.
[2] Roche Pharmaceuticals. Package Literature Kytril®. June 2001.
[3] Aventis Pharmaceuticals, Inc. Package Literature Anzemet®. October 2003.
[4] Helsinn Healthcare. Package Literature Aloxi®. July 2003.
[5] Website. Online. Internet. 2004. Available: http://www.nci.nih.gov/statistics/
[6] Gan TJ, Meyer T, Apfel C. Chung F, et al. Concensus guidelines for managing postoperative nausea and vomiting. Anesthia and Analgesia. July 2003; 97(1): 62-71.
[7] American Society of Health-System Pharmacists. ASHP Therapeutic guidelines of the pharmacologic management of nausea and vomiting in adult and pediatric patients receiving chemotherapy or dadiation therapy or undergoing surgery. Am J Health-Syst. Pharm. 1999; 56:729-64.
[8] Cochrane Pregnancy and Childbirth Group. Interventions for nausea and comiting in early pregnancy. The Cochrane Library. 2004; 2. no page number.
[9] Sullivan CA, Johnson, CA, Roach, H, et al. A pilot study of ondansetron for hypermemesis gravidarum. American Journal of Obstetrics and Gynecology. 1996; 174(5): 165-168.

APPENDIX H

Regranex® (Becaplermin) Utilization Review

Oklahoma Medicaid
September 2004

Background

Pharmacology and Indications

- Regranex® (becaplermin) is a dermatological platelet-derived growth factor.
- Becaplermin has biologic activity similar to that of endogenous platelet-derived growth factor, which includes promoting the chemotactic recruitment and proliferation of cells involved in wound repair and enhancing the formulation of granulation tissue.
- Becaplermin is indicated for the treatment of lower extremity diabetic neuropathic ulcers that extend into the subcutaneous tissue or beyond and have adequate blood supply (Stage III or IV AET Staging classification).

Dosing/Duration

- Spread a continuous layer approximately 1/16 of an inch thickness over entire ulcer surface for 12 hours per day (covered by a moist dressing).
- Reassess treatment if ulcer has not decreased in size by 30% after 10 weeks or complete healing has not occurred in 20 weeks.

Utilization – July 2003 through June 2004

For the period of July 2003 through June 2004, a total of 105 clients received a Regranex® prescription through the Oklahoma Medicaid fee-for-service program.

	# of Claims	Total Units	Total Days	Units/ Day	Total Cost	Total Clients	Per Diem
Regranex®	281	4,920	3.491	1.41	$154,009.70	105	$44.12

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

All Clients FY04

AGE	Female	Male	Totals
20 to 34	0	2	2
35 to 49	10	9	19
50 to 64	14	8	22
65 to 79	25	10	35
80 to 94	19	4	23
95+	4	0	4
Totals	**72**	**33**	**105**

Clients in Nursing Facility

AGE	Female	Male	Totals
20 to 34	0	0	0
35 to 49	1	4	5
50 to 64	5	3	8
65 to 79	12	5	17
80 to 94	14	4	18
95+	3	0	3
Totals	**35**	**16**	**51**

Total Cost FY '04	**$ 154,009.70**
Total Cost FY '03	*$ 184,322.26*
Total Claims FY '04	**281**
Total Claims FY '03	*360*
Total Clients FY '04	**105**
Total Clients FY '03	*149*
Per Diem FY '04	**$ 44.12**
Per Diem FY '03	*$ 45.47*

	7/03 thru 12/03	1/04 thru 6/04	% Change
Total Claims	133	148	11.3 ↑
Total Clients	62	67	8.1 ↑
Total Paid	$ 69,463.64	$ 84,546.06	21.7 ↑

Potential cost for Calendar Year 2004: **~ $ 170,000.00**

Analysis of Claims per Client

	Median	**Mean**	**Total**
Claims	2.00	2.68	281
Units (gms)	30.00	46.86	4,920
Day Supply	16.00	33.25	3,491
Amount Paid	$ 942.64	$ 1,466.76	$ 154,009.70
Gms/Claim	15.00	17.17	N/A
Gms/Day	1.50	1.98	N/A
Weeks of Use	2.29	4.75	N/A
Mean Ulcer Size (in)*	3.46	4.58	N/A

*Mean Ulcer Size = (Total Gm/0.4333)/Total Day Supply

Diagnosis

For the 105 clients, a total of 76 (72.4 %) had potentially relevant diagnosis information listed on medical or hospital claims for the period July 2003 through June 2004.

	Diabetes (n=105)	**Ulceration (n=105)**
Number of Clients	59 (56.2 %)	58 (55.2 %)

The remaining 29 clients were reviewed manually, 10 of these clients may have had a concurrent infection, 2 with possible cancer, and 2 with ulceration due to decreased blood flow.

	Diabetes (n=105)	**Ulceration (n=105)**
Number of Clients	9 (8.6 %)	16 (15.2%)

Although client review of this medication indicates usage in clients who may not meet the diagnostic criteria (35.2 %), and a small percentage (3.8 %) of the population continued the use of Regranex® (becaplermin) past 20 weeks of therapy, the College of Pharmacy does not recommend any action at this time, as overall usage of this medication has not increased. The College will, however, continue to monitor the use of this medication.

APPENDIX I

FDA labeled Indications

Oprelvekin (Neumega)

- Prevention of severe thrombocytopenia and the reduction of the need for platelet transfusions following myelosuppressive chemotherapy in patients with non-myeloid malignancies who are at high risk for severe thrombocytopenia

Darbepoetin Alfa (Aranesp)

- Anemia associated with chronic renal failure (on dialysis)
- Anemia associated with chronic renal insufficiency (not on dialysis)
- Chemotherapy associated anemia
- Non-FDA Cancer-associated anemia

Pegfilgrastim (Neulasta)

- To decrease the incidence of infection/febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia

Sargramostim (Leukine)

- Following induction chemotherapy in acute myelogenous leukemia
- Myeloid reconstitution after allogeneic/autologous bone marrow transplantation
- Peripheral stem cell mobilization and following transplantation
- Use in bone marrow transplant failure or engraftment delay

Epoetin Alfa (Epogen & Procrit)

- Anemia in chemotherapy-treated patients (initial)
- Anemia in zidovudine-treated HIV-infected patients (initial)
- Anemia of chronic renal failure (initial)
- Reduction of blood transfusions in surgery patients

Filgrastim (Neupogen)

- Cancer patients including acute myeloid leukemia receiving chemotherapy
- Following bone marrow transplantation
- Idiopathic, cyclic or congenital neutropenia
- Peripheral blood progenitor cell mobilization

Utilization

For the period of Jan 2002 through December 2002, a total of 429 clients received colony stimulating products through the Medicaid fee-for-service program.

Product	# of Claims	Total Units	Total Days	Units/ Day	Total Cost	Total Clients	Per Diem
Aranesp Inj 25mcg/ml	10	36	356	0.10	$3,993.16	4	$11.22
Aranesp Inj 40mcg/ml	15	60	410	0.15	$8,605.60	5	$20.99
Aranesp sol 60mcg/ML	7	28	228	0.12	$7,400.57	2	$32.46
Aranesp sol 100mcg/ml	4	16	158	0.10	$6,943.24	2	$43.94
Epogen 2000u/ml	35	193	639	0.30	$4,273.69	11	$6.69
ProCrit 2000u/ml	65	465	1,092	0.43	$10,195.73	18	$98.16
Epogen 3000u/ml	31	185	365	0.51	$6,038.02	11	$16.54
ProCrit 3000u/ml	92	540	1,352	0.40	$18,652.59	23	$13.80
Epogen 4000u/ml	74	768	2,004	0.38	$35,814.43	30	$17.87
ProCrit 4000u/ml	176	1,244	3,051	0.41	$54,313.63	35	$17.80
Epogen 10000/ml	184	1,490	4,765	0.31	$167,218.65	74	$35.09
ProCrit 10000/ml	476	2,453	8,265	0.30	$275,855.39	116	$33.38
Epogen 20000/ml	41	266	1,135	0.23	$62,631.21	16	$55.18
ProCrit 20000/ml	193	761	3,603	0.21	$176,937.12	51	$49.11
Epogen 40000/ml	19	116	637	0.18	$57,204.66	9	$89.80
ProCrit 40000/ml	220	809	4,822	0.17	$353,182.49	69	$73.24
Neupogen 300/ml	128	1,384	1,887	0.73	$231,090.96	55	$122.46
Neupogen	28	372	362	1.03	$78,694.99	9	$217.39
Neulasta 6mg/0.6ml	13	39	138	0.28	$50,993.65	11	$369.52
Leukine 250mcg	3	17	17	1	$2,300.62	1	$135.33
Neumega 5mg	6	42	42	1	$8,252.94	3	$196.50
Total FY02	**1,820**	**11,284**	**35,328**		**$1,620,593.34**	**429***	

*Total unduplicated clients for FY02

For the period of Jan 2003 through December 2003, a total of 420 clients received colony stimulating products through the Medicaid fee-for-service program.

Product	# of Claims	Total Units	Total Days	Units/ Day	Total Cost	Total Clients	Per Diem
Aranesp Inj 25mcg/ml	24	81	696	0.17	$8,722.56	9	$12.53
Aranesp Inj 40mcg/ml	6	20	119	0.17	$3,532.10	4	$29.68
Aranesp sol 60mcg/ml	23	114	1,001	0.11	$30,073.06	10	$30.04
Aranesp sol 100mcg/ml	21	74	822	0.09	$32,525.83	9	$39.57
Aranesp Inj 100mcg/0.5ml	3	12	196	0.06	$11,240.14	2	$57.35
Aranesp Inj 60mcg/0.3ml	1	3	84	0.04	$3,162.23	1	$37.65
Aranesp Inj 200mcg/ml	5	8	86	0.09	$7,041.15	3	$81.87
Aranesp Inj 200mcg/0.4ml	2	2	28	0.07	$1,791.72	1	$63.99
Epogen 2000u/ml	1	113	627	0.18	$2,842.38	7	$4.53
ProCrit 2000u/ml	59	297	997	0.30	$7,205.40	14	$7.23
Epogen 3000u/ml	24	176	559	0.31	$6,452.84	12	$11.54
ProCrit 3000u/ml	92	418	1,336	0.31	$15,006.91	24	$11.23
Epogen 4000u/ml	48	504	1,455	0.35	$24,991.22	19	$17.18
ProCrit 4000u/ml	221	1,171	3,301	0.35	$54,712.23	41	$16.57
Epogen 10000/ml	129	978	3,367	0.29	$121,088.71	48	$35.96
ProCrit 10000/ml	503	2,857	10,013	0.29	$336,600.96	137	$33.62
Epogen 20000/ml	24	201	693	0.29	$53,408.19	15	$77.07
ProCrit 20000/ml	201	1,111	5,685	0.20	$261,747.68	69	$46.04
Epogen 40000/ml	5	9	34	0.26	$4,692.54	2	$138.02
ProCrit 40000/ml	191	692	4,070	0.17	$323,867.03	63	$79.57
Neupogen 300/ml	137	1,451	2,092	0.70	$264,554.06	49	$126.46
Neupogen	30	418	531	0.79	$125,406.10	10	$236.17
Neulasta 6mg/0.6ml	5	9	83	0.11	$18,894.80	2	$227.65
Leukine 250mcg	3	24	31	0.77	$6,151.01	2	$198.42
Total FY 03	**1,760**	**10,741**	**37,822**		**$1,722,548.62**	**420***	

*Total unduplicated clients for FY03

For the period of Jan 2004 through June 2004, a total of 465 clients received colony stimulating products through the Medicaid fee-for-service program.

Product	# of Claims	Total Units	Total Days	Units/ Day	Total Cost	Total Clients	Per Diem
Aranesp Inj 25mcg/ml	38	87	556	0.16	$6,876.41	8	$12.37
Aranesp Inj 40mcg/ml	5	12	212	0.06	$2,127.47	2	$10.06
Aranesp sol 25mcg/.42ml	2	5	59	0.93	$890.55	1	$15.09
Aranesp sol 60mcg/ml	28	90	979	0.09	$23,794.80	11	$24.31
Aranesp sol 100mcg/ml	40	78	902	0.09	$34,386.20	18	$38.12
Aranesp sol 40mcg/0.4ml	1	24	56	0.43	$4,288.36	1	$76.58
Aranesp Inj 100mcg/ml	26	79	849	0.09	$50,766.45	14	$59.80
Aranesp Inj 150mcg/ml	2	8	56	0.14	$6,589.80	1	$117.68
Aranesp Inj 200mcg/ml	10	31	271	0.11	$25,453.23	4	$93.92
Aranesp Inj 60mcg/0.3ml	9	24	252	0.09	$14,591.34	2	$57.90
Aranesp Inj 200mcg/0.4ml	11	19	268	0.07	$20,002.43	4	$74.64
Epogen Inj 2000u/ml	14	27	39	0.69	$706.36	2	$18.11
ProCrit Inj 2000u/ml	17	76	288	0.26	$1,886.39	9	$6.55
Epogen Inj 3000u/ml	8	82	302	0.27	$3,066.27	6	$10.15
ProCrit Inj 3000u/ml	30	169	549	0.31	$6,122.22	12	$11.15
Epogen Inj 4000u/ml	17	182	554	0.33	$9,028.28	9	$16.30
ProCrit Inj 4000u/ml	40	262	865	0.30	$12,411.36	18	$14.35
Epogen Inj 10000/ml	64	597	2,090	0.29	$73,556.67	33	$35.19
ProCrit Inj 10000/ml	276	1,811	6,107	0.30	$215,146.07	105	$35.23
Epogen Inj 20000/ml	31	253	1,053	0.24	$67,233.25	20	$63.85
ProCrit Inj 20000/ml	167	906	4,473	0.20	$204,147.56	66	$45.64
Epogen Inj 40000/ml	15	58	181	0.32	$22,701.68	5	$125.42
ProCrit Inj 40000/ml	164	613	3,141	0.20	$291,045.91	53	$92.66
Neupogen Inj 300/1ml	68	510	1,057	0.50	$91,815.30	25	$86.86
Neupogen Inj 480/1.6ml	46	1,154	800	1.44	$189,744.13	13	$237.18
Neupogen Inj 300/0.5ml	21	176	492	0.36	$52,869.68	11	$107.46
Neupogen Inj 480/0.8ml	4	52	134	0.40	$20,029.57	3	$149.47
Neulasta 6mg/0.6ml	15	17	286	0.06	$60,817.35	7	$212.65
Leukine sol 500mcg/ml	2	7	8	0.90	$1,888.64	1	$236.08
Neumega Inj 5mg/vial	3	6	6	1.00	$1,596.45	1	$266.07
Total FY 04	**1,174**	**7,418**	**26,885**		**$1,515,580.18**	**465***	

*Total unduplicated clients for FY04

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

CY 02

Age	Female	Male	Totals
0 to 9	7	12	19
10 to 19	6	7	13
20 to 34	11	15	26
35 to 49	20	20	40
50 to 64	77	27	104
65 to 79	97	37	134
80 to 94	69	20	89
95 and Over	4	0	4
Totals	**291**	**138**	**429**

CY 03

Age	Female	Male	Totals
0 to 9	9	5	14
10 to 19	4	12	16
20 to 34	12	16	28
35 to 49	25	17	42
50 to 64	64	25	89
65 to 79	90	40	130
80 to 94	74	21	95
95 and Over	6	0	6
Totals	**284**	**136**	**420**

Total Cost CY '03	**$1,722,548.62**	**↑6.30%**
Total Cost CY '02	*$1,620,593.34*	
Total Claims CY '03	**1,760**	**↓3.30%**
Total Claims CY '02	*1,820*	
Total Clients CY '03	**420**	**↓2.10%**
Total Clients CY '02	*429*	
Per Diem CY '03	**$45.54**	**↓0.72%**
Per Diem CY '02	*$45.87*	

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

Jan 04 – Jun 04

Age	Female	Male	Totals
0 to 9	12	6	18
10 to 19	9	8	17
20 to 34	10	13	23
35 to 49	26	22	48
50 to 64	65	57	92
65 to 79	66	31	97
80 to 94	51	21	72
95 and Over	6	0	6
Totals	**245**	**128**	**373**

Jan 04-June 04 Cost	*$1,515,580.18*
Jan 04-June 04 Claims	*1,174*
Jan 04-June 04 Clients	*465*
Jan 04-June 04 Per Diem	*$56.37*

Recommendations

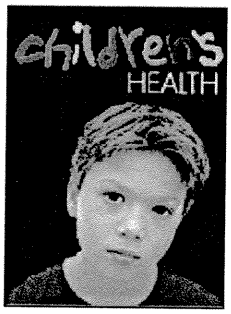
The college of pharmacy has the following recommendation (s) for Fiscal Year 2004:

At this time the use of these products seems to be appropriate and The College of Pharmacy's recommendation is to continue to monitor and regularly review the class.

APPENDIX J

ADHD Raises Risk of Substance Abuse

By Amanda Gardner
HealthDay Reporter



(HealthDay is the new name for HealthScout News.)

MONDAY, Aug. 18 (HealthDayNews) -- Children who are diagnosed with attention-deficit/hyperactivity disorder (ADHD) are more likely to use illicit drugs as adolescents.

This group is also more likely to start using at an earlier age, says a study appearing in the August issue of the *Journal of Abnormal Psychology*.

"The study confirms yet again that children with ADHD are indeed at risk for problems of greater substance abuse including cigarettes and alcohol," says Dr. Andrew Adesman, director of developmental and behavioral pediatrics at Schneider's Children's Hospital in New York City.

Oddly, though, these findings also have a silver lining. Recent studies have strongly suggested that Ritalin and other drugs not only improve symptoms of ADHD but also reduce the risk for substance abuse.

One study found that Ritalin actually reduced substance abuse by a factor of six. The current study "really speaks of the need for parents to intervene for their kids," Adesman says. "The treatment of ADHD with medication has both short-term benefits in terms of academics and attention, but also long-term benefits in terms of prevention or minimizing later risks of drug, cigarettes, and alcohol. With proper treatment, children do better socially and make more appropriate decisions."

ADHD is one of the most commonly diagnosed mental health disorders in children, affecting some 3 percent to 5 percent of school-age children. Children with ADHD are at risk for other behavior problems, including defiance and, eventually, more severe problems such as stealing and fighting.

These same conduct problems are also often linked to drug abuse. "This has led to lots of interest in whether ADHD is a risk factor for drug abuse if you don't have those

[behavior] problems," says Brooke Molina, lead author of the study and associate professor of psychiatry and psychology at the University of Pittsburgh School of Medicine.

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To try to tease out the different dimensions of the issue, Molina and her colleagues compared substance use and abuse between two groups of teenagers, the first consisting of 142 adolescents who had been diagnosed with ADHD and the second consisting of 100 controls without ADHD. All the participants were between 13 and 18 years old at the time of the study.

Inattention was assessed separately from impulsivity/hyperactivity.

In general, teenagers who had been diagnosed with ADHD in childhood were more likely to use and abuse alcohol and drugs by the time they were teenagers.

Within that group, however, those teens with both ADHD and behavioral problems were at the highest risk for substance abuse.

Also within this group, children with severe inattention (as opposed to hyperactivity/impulsivity) were most at risk to develop alcohol and marijuana problems and to become cigarette smokers by the time they reached adolescence.

However, the researchers were less sure about that finding than about the finding that children with more severe symptoms in general tended to be at greater risk.

"We do believe that severity is in general likely to be a risk factor," Molina says.

The study raises a number of questions. For one thing, Molina and her colleagues are not sure if the risk of drug abuse is a long-term one that translates into adult drug or alcohol abuse.

"Following these kids into adulthood is going to be key in determining longevity," Molina says. "The kids with persistent ADHD but no conduct problems were more likely to drink or be tobacco smokers. Is that more experimenting in teenage years that goes away, or does it persist and end up being something of concern?"

Also, researchers don't have a handle on why certain individuals with ADHD seem to be more vulnerable to drug abuse. "Not all kids with ADHD develop drug abuse, but we still don't know which kids are most likely to develop that problem," Molina says.

Then there is the issue of treatment. "The next hot-ticket item is going to be understanding the treatment ramifications for understanding drug abuse and that is still a wide open question," Molina concludes.

More information

For more on ADHD, visit the National Institute of Mental Health or Children and Adults with Attention-Deficit/Hyperactivity Disorder.

(SOURCES: Brooke S.G. Molina, Ph.D., associate professor of psychiatry and psychology, University of Pittsburgh School of Medicine; Andrew Adesman, M.D., director of developmental and behavioral pediatrics, Schneider Children's Hospital, New York; August 2003 *Journal of Abnormal Psychology*)

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FDA Talk Paper

T04-31
August 20, 2004

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

FDA Updates Its Review of Antidepressant Drugs in Children

Agency Details Plans to Present Data to Advisory Committees in September and Seek Advice on Appropriate Regulatory Actions

As part of its commitment to keep the American public fully informed about the status of its review of data concerning the use of antidepressants in pediatric patients, the Food and Drug Administration (FDA) is issuing this update to provide health care providers and patients with the most current information on this topic.

FDA has completed a new analysis of pediatric suicidality (suicidal thoughts and actions) data submitted to the agency and will be posting its analysis on its web site. FDA will also be posting on its web site additional summaries of pediatric efficacy studies from drugs that have been studied in depression in pediatric patients. Although specific new labeling language has yet to be developed, FDA will assure that the labels of the antidepressants used in pediatric patients reflect the most recent information obtained from these studies and analyses.

Next month, on September 13 and 14, 2004, FDA officials will be discussing this issue at a public meeting of its Psychopharmacologic Drugs and Pediatric Advisory Committees, at which time the agency will hear from the public and solicit the advice of the committees on these labeling changes and other possible regulatory actions.

Background

FDA has been closely reviewing the results of antidepressant studies in children since June 2003, after an initial report on studies with paroxetine (Paxil) appeared to suggest an increased risk of suicidal thoughts and actions in the children given Paxil, compared to those given placebo. Later reports on studies of other drugs supported the possibility of an increased risk of suicidal thoughts and actions in children taking these drugs. There were no suicides in any of the trials.

FDA has closely examined the studies of the antidepressants because of the potential public health impact of a link between the drugs and suicidality and the importance of these drugs in treating depression and other serious mental health conditions. On close examination of the initial reports of suicidality, it was unclear whether some of the identified suicidal behaviors reported in these studies represented actual suicide attempts or self-injurious behavior that was not suicide-related. FDA therefore arranged with Columbia University suicidality experts to review these reports.

Meanwhile, FDA brought the available information to its Psychopharmacologic Drugs Advisory Committee (PDAC) and Pediatric Subcommittee of the Anti-Infective Drugs Advisory Committees on February 2, 2004. The advisory committee members advised FDA that even before the Columbia analysis was complete, the labeling should draw more attention to the need to monitor patients closely when antidepressant therapy is initiated. Based on this recommendation, FDA asked manufacturers to change the labels of ten

drugs to include stronger cautions and warnings about the need to monitor patients for worsening of depression and the emergence of suicidality, whether such worsening represents an adverse effect of the drug or failure of the drug to prevent such worsening. The new warning language has now been added to the labels for seven of these products. Sponsors for the other three drugs have agreed to adopt the language.

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The "Columbia" Study

Because of concerns about whether the varied events identified by sponsors under the broad category of "possibly suicide-related" could all reasonably be considered to represent suicidality, FDA asked Columbia University to assemble an international panel of pediatric suicidality experts to undertake a blinded review of the reported behaviors using a rigorous classification system. The Columbia group submitted its completed review to FDA last month.

FDA has developed its analysis of the pediatric suicidality data, based on case classifications provided by Columbia University, and will be posting the analysis on its web site. While there are findings among these data suggestive of an increased risk of suicidality for some of these drugs, there remain inconsistencies in the results, both across trials for individual drugs and across drugs. Thus, an overall interpretation of these findings represents a substantial challenge.

The September FDA Advisory Committee Meeting

FDA's next step, planned for some time, will be to update the Psychopharmacologic Drugs and the Pediatric Advisory Committees about the results of these reviews and to seek assistance from the committees in interpreting the data and in considering what additional regulatory actions may be needed to promote the safe use of these drugs.

As a public health agency, FDA must weigh the possibility of an increased risk of suicidality in young patients taking these drugs against the known risk of suicide in patients whose depression goes untreated.

FDA will be bringing the following issues and draft questions to the committees for their input:

- Please comment on our approach to classification of the possible cases of suicidality (suicidal thinking and/or behaviors) and our analyses of the resulting data from the 23 pediatric trials involving 9 antidepressant drugs.
- Do the suicidality data from these trials support the conclusion that any or all of these drugs increase the risk of suicidality in pediatric patients?
- If the answer to the previous question is yes, to which of these 9 drugs does this increased risk of suicidality apply? Please discuss, for example, whether the increased risk applies to all antidepressants, only certain classes of antidepressants, or only certain antidepressants.
- If there is a class suicidality risk, or a suicidality risk that is limited to certain drugs in this class, how should this information be reflected in the labeling of each of the products? What, if any, additional regulatory actions should the Agency take?
- Please discuss what additional research is needed to further delineate the risks and benefits of these drugs in pediatric patients with psychiatric illness.

The meeting will be held in Bethesda, Maryland on September 13 and 14, 2004. So that all interested parties will have ample opportunity to review the information to be discussed next month, FDA will be posting information on its website at http://www.fda.gov/cder/pediatric/Summaryreview.htm and http://www.fda.gov/ohrms/dockets/ac/04/briefing/2004-4065b1.htm.

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2004 Safety Alert: Risperdal (risperidone)

The following information is from Janssen Pharmaceutica, Inc. Contact the company for a copy of any referenced enclosures.

Dear Health Care Provider,

Janssen Pharmaceutica, Inc. would like to inform you of important labeling changes regarding Risperdal ® (risperidone). The FDA has asked all manufacturers of atypical antipsychotic medications, including Janssen Pharmaceutica, Inc. to add a Warnings statement describing the increased risk of hyperglycemia and diabetes in patients taking these medications, including Risperdal.

Accordingly, the Risperdal Prescribing Information has been updated with the addition of the following information:

WARNINGS

Hyperglycemia and Diabetes Mellitus
Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics, including Risperdal. Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given these confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related adverse events in patients treated with the atypical antipsychotics. Precise risk estimates for hyperglycemia-related adverse events in patients treated with atypical antipsychotics are not available. Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for

worsening of glucose control.

Patients with risk factors for diabetes mellitus (eg, obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug. **119**

If you have any questions regarding this important safety information, please contact Janssen Medical Affairs at 1-800-JANSSEN. Please refer to the full prescribing information for RISPERDAL included with this letter. As always, we request that serious adverse events be report to Janssen at 1-800-JANSSEN or to the FDA MedWatch program by phone (1-800-FDA-0188), by fax (1-800-FDA-0178), or by e-mail (www.fda.gov/medwatch).

Sincerely,

Ramy A. Mahmoud, MD, MPH
Vice President, CNS
Janssen Medical Affairs, LLC

Return to 2004 Safety Summary

US Medical
Pfizer Inc
235 East 42nd Street 150/7/5
New York, NY 10017
Tel 212 573 3320 Fax 212 857 3558

Pfizer Global Pharmaceuticals

IMPORTANT PRESCRIBING INFORMATION

Dear Healthcare Practitioner:

The Food and Drug Administration requested that a warning be added to the prescribing information for all atypical antipsychotics regarding the risk of hyperglycemia and diabetes. This warning advises in part that hyperglycemia, in some cases extreme, has been reported in patients treated with atypical antipsychotics. Attached for your review is the updated full GEODON (ziprasidone) prescribing information.

The new warning provides information that is specific to GEODON, hyperglycemia, and related adverse events:

WARNINGS:

Hyperglycemia and Diabetes Mellitus
Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics. There have been few reports of hyperglycemia or diabetes in patients treated with GEODON. Although fewer patients have been treated with GEODON, it is not known if this more limited experience is the sole reason for the paucity of such reports. Assessment of the relationship between atypical antipsychotic use and glucose abnormalities is complicated by the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given these confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies, which did not include GEODON, suggest an increased risk of treatment-emergent hyperglycemia-related adverse events in patients treated with the atypical antipsychotics included in these studies. Because GEODON was not marketed at the time these studies were performed, it is not known if GEODON is associated with this increased risk. Precise risk estimates for hyperglycemia-related adverse events in patients treated with atypical antipsychotics are not available.

Patients with an established diagnosis of diabetes mellitus who are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. Patients with risk factors for diabetes mellitus (eg, obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of antidiabetic treatment despite discontinuation of the suspect drug.

While, as noted above, there have been few reports of hyperglycemia or diabetes in patients treated with GEODON, an exhaustive review of the GEODON database revealed no increased signal for diabetes. Additional information is needed to confirm this. However, as noted in the new warning, it is prudent to monitor patients treated with atypical antipsychotics for signs and symptoms of diabetes. Patients with risk factors for diabetes mellitus (eg, obesity, family history) who are starting treatment with atypical antipsychotics should undergo baseline screening and routine monitoring throughout therapy to mitigate the risk of developing serious metabolic complications. GEODON is indicated for the treatment of schizophrenia.

Pfizer continues to be committed to working with health authorities including FDA to assure that appropriate evidence-based information is included in prescribing information for GEODON (ziprasidone).

Please see accompanying full Prescribing Information included with this letter.

For additional information about GEODON, call 1-800-438-1985.

Sincerely,

Cathryn M. Clary

Cathryn M. Clary, MD, MBA
Vice President
Psychiatry, Neurology
US Medical, Customer & Markets Development

Centocor

11 August 2004

IMPORTANT DRUG WARNING

Dear Healthcare Professional:

Centocor would like to inform you of important safety information concerning hematologic and neurologic events for REMICADE® (infliximab), a biological therapeutic product indicated for the treatment of rheumatoid arthritis and Crohn's disease.

In postmarketing experience worldwide, hematologic events including leukopenia, neutropenia, thrombocytopenia and pancytopenia, some with a fatal outcome, have been reported in patients receiving REMICADE. Accordingly, Centocor has added a Warning on Hematologic Events to the labeling for the product as follows:

> **Hematologic Events**
>
> Cases of leukopenia, neutropenia, thrombocytopenia, and pancytopenia, some with a fatal outcome, have been reported in patients receiving REMICADE. The causal relationship to REMICADE therapy remains unclear. Although no high-risk group(s) has been identified, caution should be exercised in patients being treated with REMICADE who have ongoing or a history of significant hematologic abnormalities. All patients should be advised to seek immediate medical attention if they develop signs and symptoms suggestive of blood dyscrasias or infection (e.g., persistent fever) while on REMICADE. Discontinuation of REMICADE therapy should be considered in patients who develop significant hematologic abnormalities.

In addition, the Warning on Neurologic Events has been updated (see Warnings in the enclosed prescribing information) to:

- describe rare cases of CNS manifestation of systemic vasculitis; and
- warn that discontinuation of REMICADE should be considered in patients who develop significant central nervous system adverse reactions.

Centocor, Inc. · 200 Great Valley Parkway · Malvern, Pennsylvania 19355-1307 · Telephone (610)-651-6000 · Facsimilie (610)-651-6100

Finally, the Adverse Reaction sections of the REMICADE prescribing information has been updated to add the following adverse events that have been reported during post-approval use of REMICADE: neutropenia, pericardial effusion and systemic and cutaneous vasculitis.

Since August 24, 1998, when REMICADE was approved in the US, approximately 509,000 patients have been treated with REMICADE worldwide.

Enclosed please find the updated prescribing information as well as the patient information sheet.

Centocor is committed to ensuring that REMICADE is used safely and effectively and is committed to providing you with the most current product information for REMICADE. You can assist us with monitoring the safety of REMICADE by reporting adverse events to Centocor at 1-800-457-6399. Alternatively, this information may be reported to FDA's MedWatch reporting system by phone (1-800-FDA-1088), facsimile (1-800-FDA-0178), the MedWatch website at www.fda.gov/medwatch, or mailed to MedWatch, HF-2, 5600 Fishers Lane, Rockville, MD 20852-9787. Both healthcare professionals and consumers should use Form 3500 for reporting adverse events.

Should you have any questions or require further information regarding the use of REMICADE, please contact Centocor's Medical Affairs Department at 1-800-457-6399.

Sincerely,

Daniel Everitt

Daniel Everitt, MD
Vice President,
Clinical Pharmacology and Global Pharmacovigilance
Centocor, Inc.