THE UNIVERSITY OF OKLAHOMA

MEMORANDUM

TO: Drug Utilization Review Board Members

FROM: Ron Graham, D.Ph.

SUBJECT: **Packet Contents for Board Meeting – October 12, 2004**

DATE: October 6, 2004

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

Enclosed are the following items related to the October 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.**

Epocrates Rx® Drug Reference Guide Demonstration - **See Appendix C.**

Review and Discuss Anti-Dementia Drug Utilization - **See Appendix D.**

Review and Discuss Guidelines for Treating Nausea and Vomiting in Pregnancy (NVP) - **See Appendix E.**

Review and Discuss Narcotic Analgesic Drug Utilization – **See Appendix F.**

Review and Discuss Rheumatoid Arthritis Drug (DMARDs) Utilization – **See Appendix G.**

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

Future Business

Adjournment

Drug Utilization Review Board

(DUR Board)

Meeting – October 12, 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. September 14, 2004 DUR Minutes - Vote
   B. Memorandum of September 28, 2004

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

4. **Update on DUR/MCAU Program - See Appendix B.**
   A. Therapy Management Quarterly Update
   B. Retrospective DUR Report for July 2004
   C. Medication Coverage Activity Audit for September 2004
   D. Help Desk Activity Audit for September 2004

Items to be presented by Mr. Alex Easton, Dr. Whitsett, Chairman:

5. **Epocrates Rx® Drug Reference Guide Demonstration - See Appendix C.**
   A. Overview
   B. Demonstration

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

6. **Review and Discuss Anti-Dementia Drug Utilization – See Appendix D.**
   A. Utilization Review
   B. COP Recommendations

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

7. **Review and Discuss Guidelines for Treating Nausea and Vomiting in Pregnancy (NVP) – See Appendix E.**
   A. Overview of Treatment Options
   B. Review of Guidelines for Anti-emetics Use

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

8. **Review and Discuss Narcotic Analgesic Drug Utilization – See Appendix F.**
   A. Utilization Review
   B. COP Recommendations

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

9. **Review and Discuss Rheumatoid Arthritis Drug (DMARDs) Utilization – See Appendix G.**
   A. Utilization Review
   B. COP Recommendations

10. **FDA and DEA Updates – See Appendix H.**

11. **Future Business**
   A. PBPA Annual Reviews
   B. Neurontin™ Follow-Up Review
   C. MS Copolymers Review
   D. Supplemental Rebate Update
   E. SMAC Update
   F. Bladder Control Medications
   G. New Product Reviews

12. **Adjournment**

APPENDIX A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of SEPTEMBER 14, 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)		
(VACANT)		

COLLEGE of PHARMACY STAFF:	PRESENT	ABSENT
Leslie Browning, D.Ph./Clinical Pharmacist	X	
Metha Chonlahan, Pharm. D./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: David Yanchick	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., Legal		X
Lynn Rambo-Jones, J.D., Legal	X	
Rodney Ramsey; Pharmacy Claims Specialist	X	

OTHERS PRESENT:

Juanita Green, Sepracor Inc.
Greg Novarro, Sepracor Inc.
JoAnne Hargrave, Schering-Plough
Aliza Tomlinson, Janssen
Pat Evans, Bristol-Myers Squibb
Jene Hynek, Organon
Rhonda Clark, Purdue
Jeff West, Chiron
Wayne Maass, Organon
Mark Nikkel, Roche
John Rolls, OMP
Bill Corley, Bayer
Ron Schnare, Abbott
Barbara Boner, Novartis
Bryan Charlton, Sepracor Inc.
Jeff Koester, Sepracor Inc.
Tim Myers, Schering-Plough
Jeff Newton, Janssen
Karen Hanna, Johnson & Johnson
Jay Arnold, Roche
Jeff Knappen, Allergan
Colby Schwartz, Sepracor Inc
Lee Blevins, Organon
Garold Richardson, Roche
Jill Miller, TAP
Tracy Copeland, Fores
Angela Menchaca, Amgen
Christi Davis O'Brien, Astra Zeneca
Mike Wilt, State of Okla.
Jonathan Klock, GlaxoSmithKline
Matt Johnson, Takeda NA
Jeff Tallent, NAMI
Traci Miller, Sepracor Inc
Carter McBride, Bristol-Myers Squibb
Richard Ponder, Johnson & Johnson
Mike Avery, Sepracor Inc
Michelle Gaulding, Ortho-McNeil
David Barton, Organon
Greg Hoke, Wyeth
Charlene Kaiser, Wyeth
Brian Leugs, PhRMA

PRESENT FOR PUBLIC COMMENT:

Jeff Koester, Sepracor Inc.	Item No. 6
Greg Novarro, Sepracor Inc.	Item No. 6
Michael Wright, Roche	Item Nos. 5 and 7 (time waived by Mr. Wright)
Deb Israel, Roche	Item No. 5
Jim Turley, Roche	Item No. 7
Wayne Barber, consumer	Item No. 5

AGENDA ITEM NO. 1: CALL TO ORDER

1A: Roll Call

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

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 2: PUBLIC COMMENT FORUM

2A: Acknowledgement of Speakers and Agenda Item

Dr. Whitsett acknowledged Public Comment speakers as noted above.

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 3: APPROVAL OF DUR BOARD MINUTES

3A: July 13, 2004 DUR Minutes

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

ACTION: MOTION CARRIED, with two abstentions (Hollen, Whitsett).

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

4A: Therapy Management Quarterly Update

From January through June 2004, 628 waiver client profiles have been reviewed. Approval/denial/incomplete totals were noted in report submitted to the Board. Materials included in agenda packet; presented by Dr. Flannigan. Dr. Whitsett asked "How well do people out in the field know that this service is available?" Dr. McNeill asked for estimate of how many waiver clients there are?

4B: Retrospective DUR Report: May/June 2004

Narcotics/Females 30-40 years was selected for retrospective review for May 2004. Pharmacy and physician response was 70% and 61% respectively. Narcotics/Males 30-40 years was selected for retrospective review for June 2004. Pharmacy and physician response was 71% and 37% respectively. Materials included in agenda packet; presented by Dr. Flannigan.

4C: Medication Coverage Activity Report: July/August 2004

The July 2004 activity audit noted total number of petitions submitted was 13,813 including super-PA's and special circumstance PA's. The August 2004 activity audit noted total number of petitions submitted was 16,132 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: July/August 2004

Total calls for July 2004 numbered 16,662 (87.7% pharmacies, 7.4% clients, 1.8% physicians, 3.1% other). Total calls for August 2004 numbered 17,563 (86.9% pharmacies, 7.6% clients, 1.5% physicians, 3.6% other). Monthly reports included in agenda packet; presented by Dr. Browning.

ACTION: NONE REQUIRED.

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

For Public Comment, Deb Israel: *I'm Deb Israel. I'm a Pharm D and liaison with Roche and personally thank you for the opportunity to get up and address the committee. And also I'd like to commend the committee for putting together some evidence based criteria for Fuzeon™. I would like to address the possibility of a few changes based on some newer data that you might not have had access to. The first one is the CD4 cell count of less than 200 as need for a prior authorization. As you might be aware, our pivotal data which was from our TORO trial had no CD4 cell cutoff. The actual range in that trial was quite wide. It was about zero to 900. And what we have found out from our latest data that was presented at the World AIDS Conference in Bangkok was that there are consequences for delaying therapy with Fuzeon™. And so there's a concern about allowing the CD4 cell count to drop too low before you start the drug. And what the data did show was that for patients who, who did delay receiving Fuzeon™, those who received Fuzeon™ remained on it, and then those who just got optimized background, failed their optimized background and then received Fuzeon™. Though they had response to Fuzeon™, it was not as robust either virologically or immunologically than if they had received Fuzeon™ earlier. So as we evolved the data, there does appear to be at least an issue if we delay therapy. And so the concern would be is that if you allow the CD4 cell count to get to 200 and not start therapy earlier, that you might not get as good a response as you might otherwise. So based on sort of typical information that's out there from consensus recommendations, we would recommend maybe going to a CD4 cell count of 350. That does tend to be a trigger for changing treatment in these patients. And so that would be one recommendation we would offer as consideration.*

Dr. Whitsett: *Let me interrupt here. And is that data published?*

Deb Israel: *Yes. I have data that I can send you . . . yes . . . from the World AIDS Conference. So as I said I will actually make all this data available to the committee. The next thing would be the need for two active agents. I think those of us who treat HIV, have involvement with HIV, understand the challenges interpreting resistance testing. I think it can be a very gray area. And some of our early data did show that the biggest step in activity was going from no active agents to one active agent. And actually based on the consensus recommendations that came out from AIDS in January, it actually said that the availability of only having a single active agent should not be a contraindication to starting Fuzeon™. So though we would prefer that patients have at least two active drugs before starting Fuzeon™, it is clear that even with one active agent, when you add Fuzeon™ on you can get a response. So the recommendation would be to actually have the ability to have at least one active agent on the checkbox for that issue. And the final thing I'd like the committee to consider and though I didn't see it on the statement, this was the issue about concern over reevaluation at six months. And I don't know how the committee is going to actually do that, but I did see or note that it was really based on at least a one log drop having virological improvement. And again, from a clinician's point of view, the other parts that take into account the CD4 cell count, and that you might have an immunologic response and maybe not a good virological response, but even if you can maintain CD4 cell counts, or even improve CD4 cell counts, even alone as a factor, the clincian may be inclined to want to keep the patient on the drug because they're stable immunologically. And if you can avoid all the consequences of immunological failure, then you're helping the patient. So what I would ask the committee to do, is to evaluate when the six months is up and there is an evaluation of that therapy, to not just use biological endpoints . . . to also look at immunological endpoints as a separate entity. And just to finish up . . . again, I appreciate the opportunity to talk and as I said, I can certainly provide all the references needed to follow up on this data. And if there are any questions . . . ?*

Dr. Whitsett: *What percent of patients do you think would at some point would be a candidate for this medication?*

Deb Israel: *Well, you know that what we have found out, as patients move through the treatment paradigm with HIV, the biggest bang for the buck is that first line therapy. So the average length is about 18 to 24 months. And each subsequent, and then throughout that patients fail therapy at some point in time, so then they go to their second line, which is shorter, and then third line therapy which is even shorter. So the eventuality is that, that patients will at some point probably need Fuzeon™. Now with it available, it allows* ***(inaudible)*** *to be strategic about where they use it, so what we're seeing now with our data is instead of that failure at third line being shorter, we're prolonging that time where patients don't fail that therapy with Fuzeon™. So to answer your question, many patients eventuallly need salvage therapy and Fuzeon™, though not necessarily salvage, they may end up on it, but now that they can use it a little bit earlier on, we can probably avoid some of the end stage things at this point in time.*

Dr. Whitsett: *And how early do you imagine it might be used?*

Deb Israel: *Well, you know we, we're still looking at that data. We have studies now and we're looking at it in the* ***(inaudible)*** *patients that maybe are naive to non* ***(inaudible)*** *or another class, it's certainly not going to be first line therapy. But we are starting to see patients that once they fail a second line drug, second line therapy, the clinicians are starting to use Fuzeon™. Because the whole idea then, is that you're not waiting until they have only one active drug. You're not waiting until their immunologic system is so far depressed and they can't respond. So it's becoming more of a third line drug, and that's again, that's the data. That's what the data's evolving to.*

Dr. McNeill: *What do other states do with Fuzeon™, as far as P.A.?*

Dr. McIlvain: *There are other states that P.A. it. I know of at least two. I have their P.A. forms, but there are probably others. And most AIDS drug assistance programs prior authorize it but they just can't afford to cover this drug* ***(inaudible).***

Dr. Whitsett: *It is expensive?*

Dr. McIlvain: *It's about $20,000 a year, plus their other HIV drug that goes on top of their other drugs that are already being paid for.*

Deb Israel: *Yeah, it is added onto other drug therapy. Nothing is monotherapy.*

Dr. Whitsett: *No discounts at that point.*

Dr. McNeill: *Why in a year and a half have only 58 claims been made on this drug?*

Dr. McIlvain: *Partly it's got availability problems, partly it hasn't been marketed as heavily in the past and now they're starting to pick up the marketing, and partly because it's just new to the doctor who has been prescribing these patients.*

For Public Comment, Wayne Barber: *First of all I want to say I am a consumer and a gentleman who is living with AIDS. It is my understanding that the committee is wanting to limit the number of individuals who are going to be able to be on Fuzeon™. I am here tonight to try to convince you otherwise. Fuzeon™ right now is known in the AIDS population as being a medicine of last resort due to its' high cost. A lot of people that are put on it, because of its' cost, is the last drug that they have. It's medication right now that we, that all we . . . that those of us know of that does show a big improvement, it does work, and extends the life of those of us who are positive. And the fear of hearing the doctor saying that you're going to go on Fuzeon™ and then to find out that the State's saying you're going to have to be put on a waiting list now. And not knowing how many years is that waiting list going to be. Are you going to have to wait until someone who on that list dies of AIDS before you're eligible to be even put on it? So I'm here to beg all of you on the committee to . . . not to cap it for those of us who are going to be depending on it, and . . . I had a whole list of things I was going to say until I got up here . . . I'm kind of nervous. Right now we've been hit hard as far as drugs, of being able to get the drugs. Those of us who are on disability and having to pay for our medications, it limits us big time. And the thought of even trying, you know, it's like the State is now saying we don't care about you. We prefer that you just crawl under the rug and just die. You're not going to get the last medication that even stands a chance to keep you alive. And nobody needs to even go through that. It's bad enough living with HIV and AIDS and living with the stigma that goes along with it, without having to find out that you're not able to get the medication that you need to keep you alive because that the State don't care no more. That's all I've got to say. Thank you.*

Dr. Whitsett: *Are there questions of Mr. Barber? The point of clarification, you had mentioned that the State was putting a cap on the number of individuals who would be eligible. Now that's not, I don't think that's so. There are an infinite number of people who could be on that. There is no cap. There's certain criteria at this point that the Oklahoma Health Care Authority, the DUR Board is looking at and see if it's used appropriately, because as an extremely expensive medication, you can imagine if it were used inappropriately what would happen . . . I don't think the State has any vendetta against people who qualify for this medication and want to make it available to the appropriate people, and that's what we're trying to work through is identify and discern those who are genuinely appropriate and make it available for them and not pull the reins in. Now at a time when things are evolving, as far as indications and, Ms. Israel gave us some new information that we haven't had, those things we take into consideration and you don't always have that when you start out on your journey to make decisions, so I think it's an evolving understanding of what's the appropriate use of this medication and we sure don't want you and others that you know to go away thinking that we intentionally want to withhold something from people who need it. That's not what we're here for. Any other questions or comments? If not, thank you very much Mr. Barber.*

Materials included in agenda packet; presented by Dr. McIlvain. Ms. Israel provided additional information and responded to questions from Board members.

Dr. McNeill moved not to prior authorize Fuzeon™ and carefully monitor it and bring the issue back to the DUR Board in six months; motion seconded by Dr. Swaim. Dr. Hollen suggested provider education starting now through letters to specific prescribers reminding them of monitoring guidelines.

ACTION: MOTION CARRIED.

AGENDA ITEM NO. 6: REVIEW & DISCUSS XOPENEX™ UTILIZATION

For Public Comment, Jeff Koester: *My name is Jeff Koester. I'm the medical liaison with Sepracor. I just had a couple of comments to make. Number one, regarding differentials between Xopenex™ and racemic albuterol. There was recently a study that was published or presented at the American Thoracic Society looking at over 600 patients with acute asthma presenting to the emergency room. They were randomized with either Xopenex™ 1.25 mg, or racemic albuterol at 2.5 mg, and Xopenex™ provided superior bronchodilatation, both at first dose and throughout*

the course of the study. So there is differential and this agrees with other data that have been developed within this particular data set, that is acute asthma. Secondly, I noticed within the recommendations there is . . . there were some recommendations about age restrictions with Xopenex™. I just wanted to make the Board aware that there are data that document it down below the age of six. Now I realize our package insert says age six, but I just want to make sure the data are out there for your . . .

Dr. Whitsett: *Published data?*

Mr. Koester: *Published data. Should I go ahead, or . . .? OK. There were two studies. One in the management of chronic outpatient asthma. They looked at Xopenex™, .31 mg and .63 mg. Patients were included down to the age of four. The second study was a study conducted at Rainbow Babies & Children's Hospital in Cleveland looking at Xopenex™ 1.25 mg in the treatment of acute asthma presenting to the emergency room. That included patients down to the age of one. Now the mean in that particular study was age seven, but the authors in either study declined, or I should say, they saw, did not see fit to differentiate because there appear to be no data that showed responses in patients below the age of six were different than at any other age of patients. And that's all I have to say.*

For Public Comment, Greg Novarro: *Thank you. If I'm redundant because Dr. Flannigan hasn't gone yet, I'm sorry. It's just difficult doing this when I haven't heard what you're going to say yet, but I've read your report. Good evening, and I want to thank the Oklahoma Health Care Authority and the DUR Board for allowing me the opportunity to speak with you regarding Xopenex™. My name is Greg Novarro. I'm the account director for Sepracor Pharmaceuticals and I first want to acknowledge that I am as proponent of preferred drug lists and believe that if states and pharmaceutical manufacturers work together, that access to medications can be made readily available to physicians and patients and overall health care costs can be reduced. And I have to commend Nancy Nesser and Dr. Flannigan and her staff at the University of Oklahoma pharmacy department for their efforts in working together to meet these goals. I travel all over the United States and believe me, my wife is not real happy with me because I travel all over the place and neither are my three children. But this is without a doubt, the most fair, balanced review that I have ever seen . . . one that is based on clinical guidelines actually used, and promotes open access to rescue medications. And I just want to thank you for that. What you're considering tonight is not just another P.A. on a medication. You are considering the lives of asthmatic children. I don't say this to make a fear point or anything like that, but fifteen children do die every day in the United States from asthma, and there is no correlation between asthma severity and death, which means even mild asthmatics can die from their disease. I cannot make the claim that Xopenex™ saves more lives than albuterol, because that study would be unethical to perform. However, we have demonstrated that Xopenex™ is a more potent bronchodilator in both the in-patient and out-patient setting. We've shown that if patients are on racemic albuterol and go to the E.R., they are 50% more likely to be admitted than if they're on nothing at all. We have shown that Xopenex™ in lower doses reduces side effects but does not compromise efficacy. We've also shown both in animal and human airway cell models that S-albuterol may be worsening the effects of asthma and making it harder to control and you will hear those, hopefully those things from the pharmacy presentation. I also want to point out that the increase in utilization that has, that you've seen is, I think, mainly due in the increase of available patients shifted from the managed Medicaid environment now over to fee-for-service Medicaid. And this is also emphasized in our market share, and it has stayed consistent but our units have grown. The point is that there is not this huge shift in use of Xopenex™ as it presented to the total market. Many of these patients may have been on Xopenex™ already in their managed Medicaid environment. Another point I want to make is Xopenex™ is not used every month. The average refill for Xopenex™ is only two times per year, nationally, and that's right in line what is in the state of Oklahoma. So, you don't get it where patients . . . and those that are using it every month will be helped out with I think recommendation number one and number two that they made. So that they're overutilizing either Xopenex™ or racemic albuterol, that should not happen . . . it's not within the guidelines. I'm in full agreement that access must remain open for this product and the guidelines should be adhered to stringently. And that's why I agree that the recommendation point number one and number two are the most logical sense and can help achieve open access . . . promote proper utilization for Xopenex™, allow for rescue utilization and promote national guidelines. No other state has put an age restriction on Xopenex™ utilization under the age of 18. This would be a first. The main point is if you choose to restrict age utilization on Xopenex™, then the only alternative to these patients is racemic albuterol. Your own utilization shows that most patients taking this drug are in one to five year olds. The main reason they are probably on Xopenex™ is because of the lower incidence of side effects and many doctors may have had these patients on albuterol in the past and they may have already failed. If you put an age restriction on Xopenex™, then the only alternative will be 2.5 mg of albuterol. Even though albuterol comes in lower doses, doctors don't use it, because lower doses do reduce the side effects from albuterol, but the efficacy is compromised. And this has been in shown clinically in our Milgrom study, so the only way to reduce side effects and not compromise efficacy with short acting beta agonists is for doctors to use Xopenex™. Forty-three other states do not have a restriction on this medication, and just yesterday the Minnesota DUR Board also chose not to have a P.A. on*

this medication. I encourage you not to put any age restrictions on this medication and please choose point number one or two which we would be in full agreement on. Any questions?

Dr. Whitsett: *Questions? You seem very positive with this medication and the data looks good. We're going to hear more about it. Is it your suggestion that we forget about racemic albuterol.*

Mr. Novarro: *Not at all. No.*

Dr. Whitsett: *And go only with this compound?*

Mr. Novarro: *No, if that's how I was coming across, no, not at all. Would I like that to happen? Sure. But no, that's not what I'm recommending. I really believe that, you know, there's . . .*

Dr. Whitsett: *A lot of people do respond to racemic albuterol and they get a good response and they're happy with that.*

Mr. Novarro: *Sure. And my thing is, let the doctors decide. That's what I'd like to see would happen, is the doctors decide. A P.A. in that situation, you're talking about minutes when it's asthma, so someone doesn't respond to racemic albuterol and they can't get a hold of their doctor and they can't get . . . and it's late at night when nocturnal symptoms usually occur with asthma, they're going right to the E.R. and if they're on albuterol, they're 50% more likely to get admitted, our studies are showing. So the doctors have the access to the medication and they, doctor had decided that Xopenex™ was better for that patient than . . . I'm . . . we're just saying, to keep that access open for what the doctor decide. . . to have a more potent drug on hand when they have the attack. But yeah, I'm not advocating for Xopenex™ instead of racemic albuterol.*

Dr. Whitsett: *Because a lot of people still respond to racemic albuterol. Generally people who are resistant are not suddenly resistant at this moment in time unless there's some precipating factor, and that needs to be addressed. Not just another bronchodilator . . . there's infection or some other factor . . . deteriorate. So if a person chronically developing a resistance to albuterol then they should report that to their doctor and they have a time to deal with that.*

Mr. Novarro: *That's true, but the data shows that S-albuterol takes 12 to 24 hours to get out of somebody's system. Let's say they come into contact with that trigger when they're out in the home. And you don't know when that's going to happen. Asthma attacks can occur at any moment. So if they start taking their albuterol and they've been taking it for awhile and all of a sudden, they take more and more and more, and they're puffing away on their either nebulizer inhaler, they're going to get a lot of S-albuterol in their body. And that's going to be harder to turn that patient around. So it could happen all of a sudden that they start negatively reacting to S-albuterol, dependent upon the amount of allergens they get in their body. We don't know. And the point is . . . you don't want S-albuterol in their body, so if Xopenex™ was available for that patient, for the doctor to decide that he would rather have them on there then, that's we would say.*

Dr. McNeill: *In looking at the charts here, I guess you've had access to these?*

Mr. Novarro: *Yes.*

Dr. McNeill: *Twenty-five percent of the utilization is in children less than one. Why? Is this during RSV season, is this in the* ***(inaudible)****, or is there . . . this is not asthma, so what, what is, why are they using . . .*

Mr. Novarro: *The data is consistent with racemic albuterol too. I think it was 28% actually, of people under one. (inaudible) as well, and if you're asking me why doctors put people on bronchodilators that are under one years old, I don't know.*

Dr. McNeill: *I meant, there's no specific . . . I know that there's no (inaudible) reason for it, but . . .*

Mr. Novarro: *Could be patient reason, could be for any reason. Pediatric pulmonologists use it for bronchiolitis, they use it for RSV. It's, like your . . . some think it's asthma at that point in time . . . I don't know. It's indicated for bronchoconstriction, or bronchospasm, so if a patient, a little baby is having bronchospasm, they're going to give either racemic albuterol orXopenex™.*

Dr. Whitsett: *And your current indications, is there an age cutoff now on that? The recommendation.*

Mr. Novarro: *The recommendations start at age six.*

Dr. Whitsett: *Age six, OK. And there may be data forthcoming that could change that, but right now, that's your package . . . ?*

Mr. Novarro: *That's what our package insert says.*

Dr. Whitsett: *Alright. And the cost of this compared to racemic is similar?*

Mr. Novarro: *No, if it was, I wouldn't be talking to you right now. And I do want to point out, and Nancy and I disagree on this point, is that the calculations of the math of the per diem is correct. The way the math is done is correct, but to let you know that one prescription often lasts a patient six months, and so it's not intentionally misleading, it's just . . . it would seem like if somebody was on Xopenex™ for more than this period of time that doctors write it, usually in 48 units, would last for two weeks. Yeah, it would cost you $8.00 a day, but they aren't using it that long. They aren't using it for a full month's period of time, because $8.00 a day times a month would be $240.00 a month, and nobody's doing that. So six months is usually the time period that one prescription lasts and. .*

Dr. Graham: *How do you know that?*

Mr. Novarro: *Because your data shows that. Of the average claim per patient is two per year . . . two prescriptions per year. So I calculated it out and I averaged about 37¢ a day. So and that happens and I can answer that question for you, why that happens is, when somebody has an attack, a doctor will give them either racemic albuterol or Xopenex™ and tell them to take it a lot in the first couple of days and then after a week, says taper off and then stop. So what happens is that usually needed in the Fall and in the Spring, you only need it for all week or two weeks at a time. And hopefully, your main goal, get that patient better faster, and keep them out of the hospital. Reduce hospitalizations. And Xopenex™ in our studies has shown to that better than racemic albuterol.*
Dr. Hollen: *So a clarification based on what you just said, if we do number two recommendation, which is allow for 90 days of therapy, is that consecutive 90 days so that if the patient only needed two prescriptions for the year, would that then require that second prescription, if it fell outside the 90 days, would require a P.A.?*
Dr. Flannigan: *I had in mind it was how we had the benzo therapy . . . for those that . . .*
Dr. Nesser: *Yeah, if you send in a script for Xopenex™ with 30 days, that's 30 days on your tab. And then it could be the next month or it could be in six months, and you'd get another script with a 30-day supply, so then . . .*
Dr. Hollen: *So there's a way to say, per year? OK.*
Mr. Novarro: *And that's a good adherence to the guideline, too.*
Materials included in agenda packet; presented by Dr. Flannigan.
ACTION: NONE REQUIRED.

AGENDA ITEM No. 7: **REVIEW & DISCUSS HEPATITIS C AGENTS UTILIZATION**
For Public Comment, Jim Turley: *Thank you Dr. Whitsett. I'm a clinical specialist for Roche in hepatology and I reviewed the document that was prepared by Dr. Moore and I found it well written. At this time, I'd just like to inform the Committee that I would be glad to be used as a resource for this for future discussions. Thank you.*
Materials included in agenda packet; presented by Dr. Moore.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 8: **REVIEW & DISCUSS RESTASIS™ UTILIZATION**
Materials included in agenda packet; presented by Dr.Le.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 9: **REVIEW & DISCUSS ANTI-EMETIC UTILIZATION**
Materials included in agenda packet; presented by Dr. Le. Dr. Whitsett requested that more data and information be brought back to the DUR Board describing number of scripts and how long the use is for these clients.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 10: **REVIEW & DISCUSS REGRANEX™ UTILIZATION**
Materials included in agenda packet; presented by Dr. Gorman.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 11: **REVIEW & DISCUSS COLONY STIMULATING FACTOR UTILIZATION**
Materials included in agenda packet; presented by Dr. Browning.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 12: **FDA & DEA UPDATES**
Materials included in agenda packet; presented by Dr. Graham. Dr. Whitsett requested more review of antidepressants use in children along with the FDA reviews.

ACTION: NONE REQUIRED.

AGENDA ITEM No. 13: **FUTURE BUSINESS**

13A: RA Medications Review
13B: Antidementias Review
13C: Benzo/Ambien™ Follow-Up Review
13D: Growth Hormones Review
13E: Neurontin™ Follow-Up Review
13F: MS Copolymers Review
13G: Supplemental Rebate Update
13H: Narcotic Analgesic Review

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

AGENDA ITEM No. 14: **ADJOURNMENT**

The meeting was declared adjourned.

The University of Oklahoma College of Pharmacy

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

Memorandum

Date: September 28, 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 September 14, 2004.

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

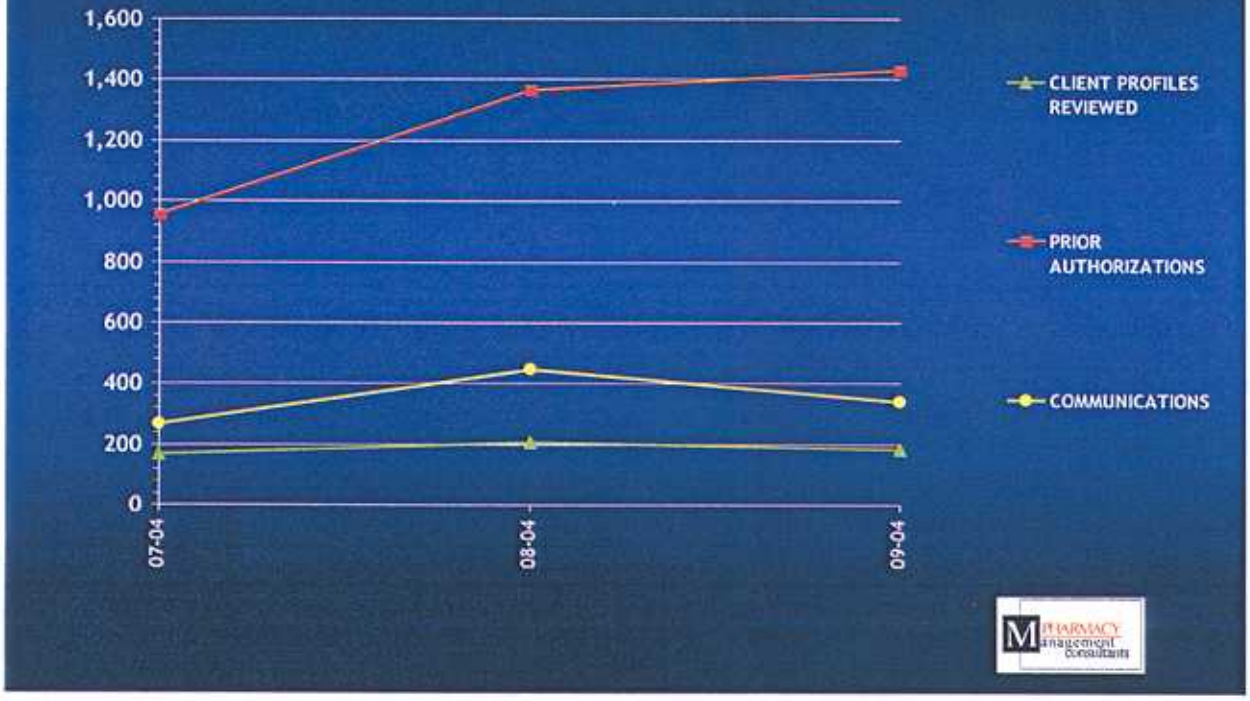
The DUR Board moved not to prior authorize Fuzeon™ and carefully monitor it and bring the issue back to the DUR Board in six months for follow up review. MOTION CARRIED.

APPENDIX B

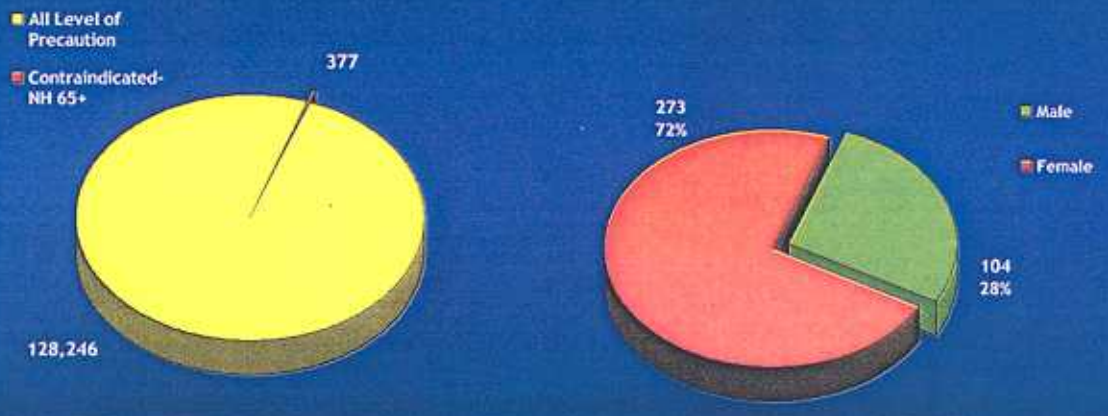
Pharmacotherapy Management Program
Quarterly Report
July – September 2004
Oklahoma Medicaid

	CLIENT PROFILES REVIEWED			PRIOR AUTHORIZATIONS				COMMUNICATIONS	
Month	New Clients	Established Clients	Incomplete Information	Total	Approved	Denied	Incomplete	Letters	Calls
July 2004	80	61	26	478	290	18	170	236	32
Aug 2004	102	77	27	681	381	24	276	348	100
Sept 2004	114	46	23	714	401	44	269	234	104
Oct 2004	0	0	0	0	0	0	0	0	0
Nov 2004	0	0	0	0	0	0	0	0	0
Dec 2004	0	0	0	0	0	0	0	0	0
Jan 2005	0	0	0	0	0	0	0	0	0
Feb 2005	0	0	0	0	0	0	0	0	0
March 2005	0	0	0	0	0	0	0	0	0
April 2005	0	0	0	0	0	0	0	0	0
May 2005	0	0	0	0	0	0	0	0	0
June 2005	0	0	0	0	0	0	0	0	0
Totals	296	184	76	1,873	1,072	86	715	818	236
1st Quarter	296	184	76	1,873	1,072	86	715	818	236
2nd Quarter	0	0	0	0	0	0	0	0	0
3rd Quarter	0	0	0	0	0	0	0	0	0
4th Quarter	0	0	0	0	0	0	0	0	0
Totals	296	184	76	1,873	1,072	86	715	818	236

PHARMACOTHERAPY QUARTERLY REPORT
July - September 2004

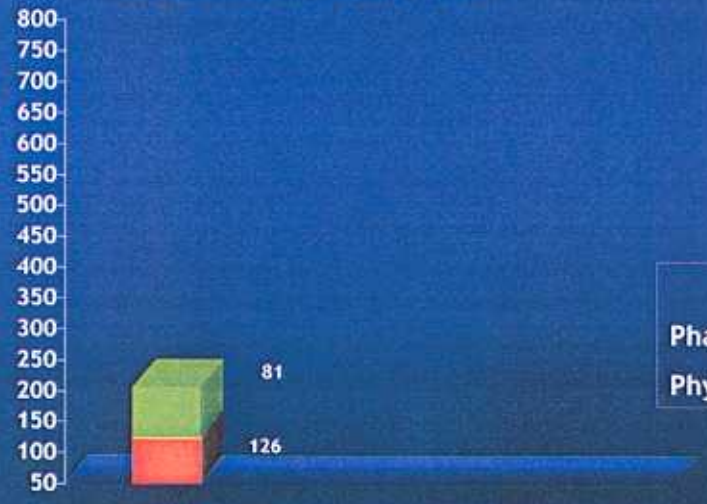


Oklahoma Medicaid RetroDUR Activity Report
July 2004 Drug-Disease Level - Contraindicated
Nursing Home Females over 65 years of age



Oklahoma Medicaid RetroDUR Activity Report
Follow Up
July 2004 Drug-Disease Level - Contraindicated
Nursing Home Females over 65 years of age

Total Clients Reviewed = 207



Total Responses		
Pharmacy =	10/82	12%
Physician =	11/76	14%

Activity Audit for

September 01 2004 Through September 30 2004

Date	Antiulcers		Anxiolytic/ Hypnotics		Antihistamine		Growth Hormones		Stimulant		Smoking Cess.		Nsaids		ACE Inhibitors		HTN Combos		Calcium Channel Blockers		Plavix		NPA		Misc		Daily Total
	app.	den.	app.	den.	app.	den.	app.	den.	app.	den.	app.	den.	app.	den.	app.	den.	app.	den.	app.	den.	app.	den.	app.	den.	app.	den.	
1	5	14	198	30	34	32	1	0	89	10	0	0	11	22	1	3	3	1	1	7	27	6	18	17	0	3	533
2	11	41	221	20	49	39	0	0	76	23	0	0	11	22	3	10	2	2	6	12	30	14	9	15	0	3	619
3	3	19	190	34	33	38	0	0	93	34	0	0	11	27	0	1	3	2	0	7	21	4	14	10	1	1	546
4	1	8	58	17	12	10	0	0	26	10	0	0	4	10	0	2	0	1	1	4	9	3	0	7	0	0	183
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	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
7	5	24	201	19	63	27	1	0	47	20	0	0	9	23	3	5	1	3	7	13	28	7	11	8	0	0	525
8	8	24	206	32	62	51	0	0	69	36	0	0	20	17	3	2	2	1	4	13	30	7	16	15	0	2	620
9	12	14	231	47	66	47	0	0	82	37	0	0	7	29	2	5	4	1	3	6	34	7	27	16	0	0	677
10	4	30	156	26	45	41	2	0	71	26	0	0	15	37	1	10	1	3	5	18	20	10	13	24	0	0	558
11	1	5	21	6	5	5	0	0	23	8	0	0	5	8	0	0	0	0	0	0	6	0	2	0	0	0	95
12	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
13	3	16	171	30	35	27	3	0	79	18	0	0	4	21	2	4	3	1	4	14	23	16	8	13	0	0	495
14	3	18	154	37	38	60	0	0	94	46	0	0	19	35	3	2	3	3	3	10	30	13	21	11	0	0	603
15	3	17	202	34	54	25	0	0	105	40	0	0	13	28	3	2	2	2	11	15	28	12	21	8	0	1	626
16	6	17	142	34	52	41	0	0	97	25	0	0	20	25	3	5	4	3	8	18	16	9	31	20	0	0	576
17	6	13	174	38	27	39	5	0	79	43	0	0	10	36	1	2	3	0	9	8	25	10	15	18	0	2	563
18	1	1	37	4	15	12	0	0	19	5	0	0	3	12	0	2	0	1	0	5	5	3	0	1	0	0	126
19	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
20	4	8	162	25	43	24	0	0	78	36	0	0	9	14	1	1	0	2	4	9	17	6	26	8	0	0	477
21	8	13	159	36	60	34	0	0	87	37	0	0	16	19	2	8	2	2	8	12	19	12	19	4	0	1	558
22	2	26	161	34	46	43	3	0	101	25	0	0	13	28	0	10	0	3	3	16	28	8	17	10	0	1	578
23	6	18	144	23	69	44	2	0	92	30	0	0	21	15	5	2	1	1	3	8	25	8	26	17	0	2	562
24	6	18	147	34	38	38	0	0	70	27	0	0	7	30	4	10	1	4	3	8	21	6	36	15	0	3	526
25	0	4	41	4	17	7	0	0	29	8	0	0	1	12	0	2	2	0	2	3	2	4	0	1	0	1	140
26	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
27	8	10	145	26	43	32	3	0	71	33	0	0	13	26	4	5	2	2	6	9	25	5	38	20	1	1	528
28	9	23	142	25	49	38	1	0	94	41	0	0	7	36	1	8	4	2	3	10	24	9	72	15	0	1	614
29	10	23	146	16	47	31	1	0	96	23	0	0	9	27	0	5	3	1	4	11	22	4	53	10	0	3	545
30	8	13	114	27	49	37	0	0	100	37	0	0	4	35	3	3	2	2	5	7	14	8	43	15	1	3	530

Activity Audit for

September 01 2004 Through September 30 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.	133		3723		1051		22		1867		0		262		45		48		103		529		536		3		
Den.		417		658		822		0		678		0		594		109		43		243		191		298		28	
Average Length of Approvals in Days	104		100		107		159		273		0		336		349		350		342		267		174		81		

Smoking Cessation

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

Changes to existing PA's	1198
Total (Previous Year)	9918

Monthly Totals

	Number	Percent of Total
Approved	8445	51.79%
Additional PA's	15	0.09%
SUPER PA's	1381	8.47%
Emergency PA's	7	0.04%
Duplicates	1126	6.91%
Incompletes	1171	7.18%
Denied *	4160	25.51%
Total	16305	100.00%

Daily Average of 652.20 for 25 Days

*** Denial Codes**

762 = Lack of clinical information	30.84%
763 = Medication not eligible	1.95%
764 = Existing PA	16.92%
772 = Not qualified for requested Tier	9.50%

SUPER PA's

Early Refill Attempts	59688
Dosing Change	583
lost/stolen/broke	138
Other	114
wrong DS	88
Quantity vs. Days Supply	443

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)

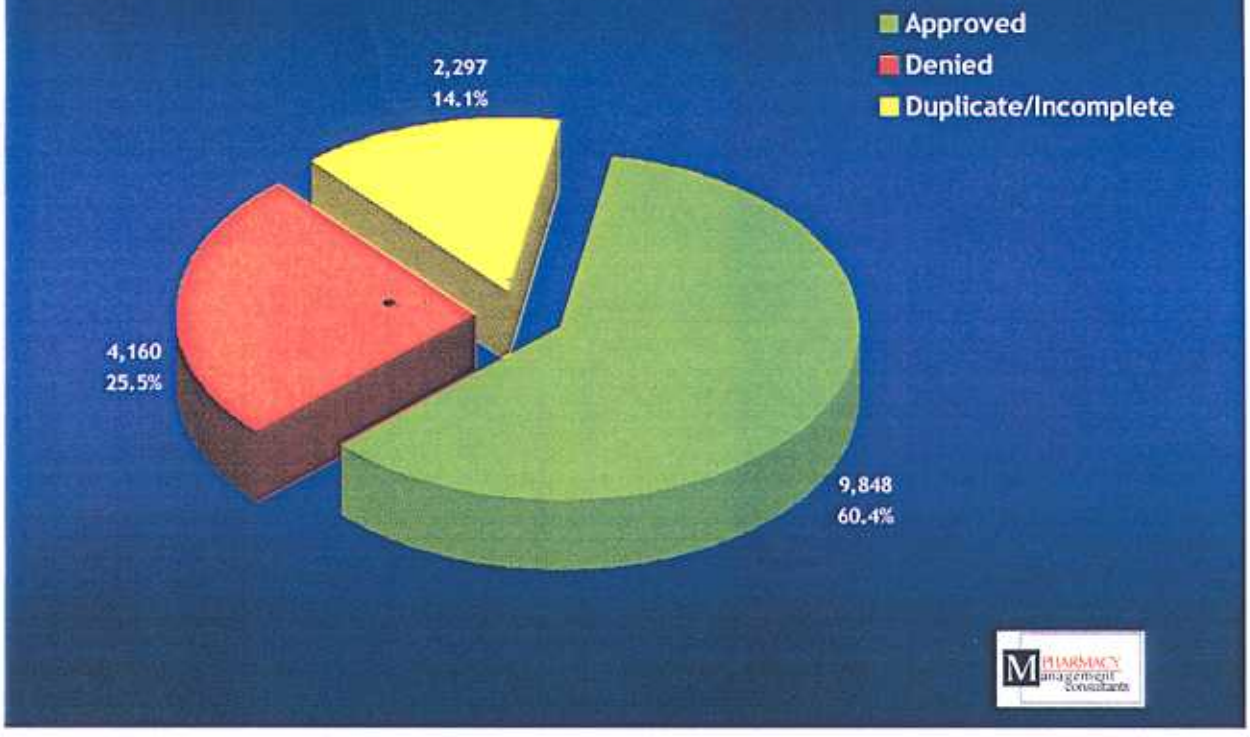
Incompletes: Missing necessary information (NDC, SIG, Diagnosis, etc.)

PRIOR AUTHORIZATION ACTIVITY AUDIT

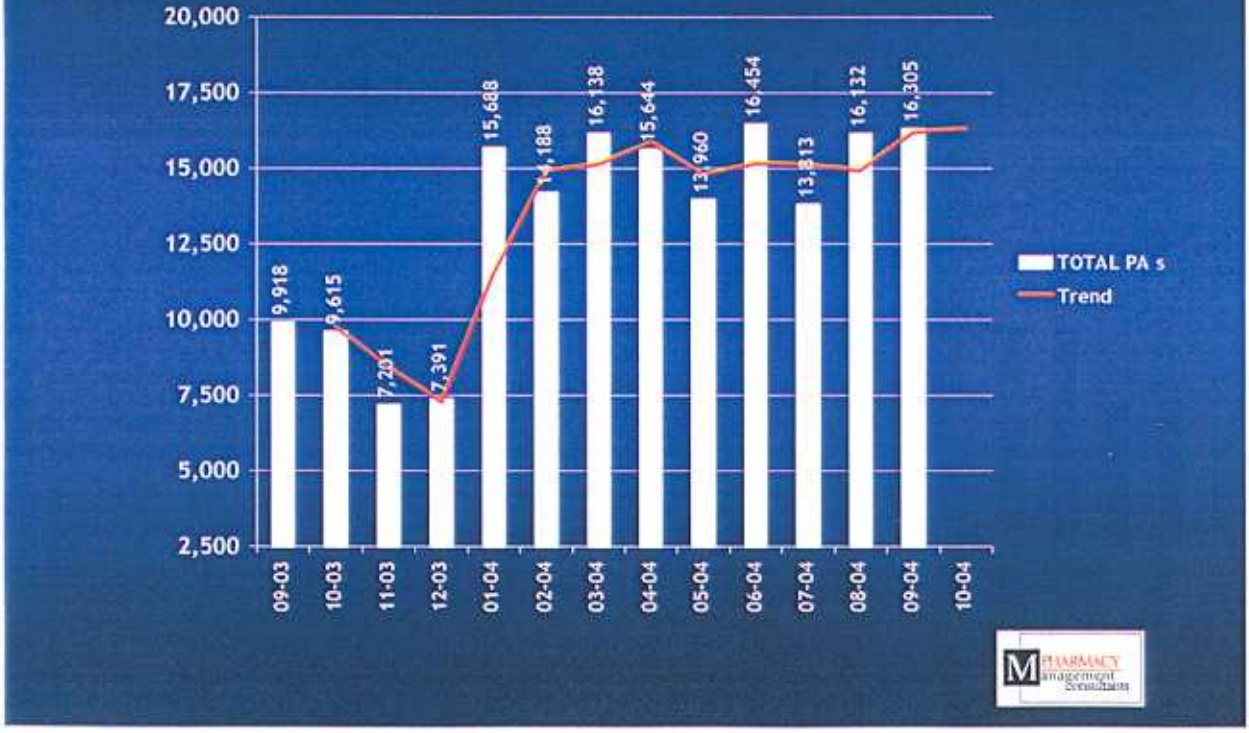
Monthly Totals

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	16,305
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**	**138,322**

PRIOR AUTHORIZATION ACTIVITY REPORT
September 2004

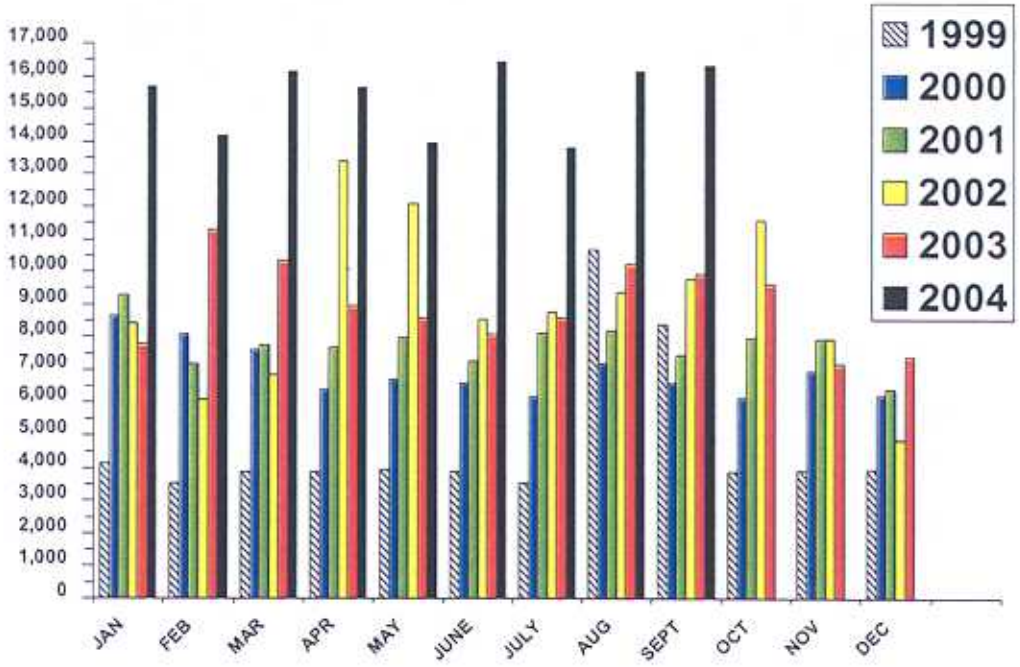


PRIOR AUTHORIZATION REPORT
September 2003 - September 2004



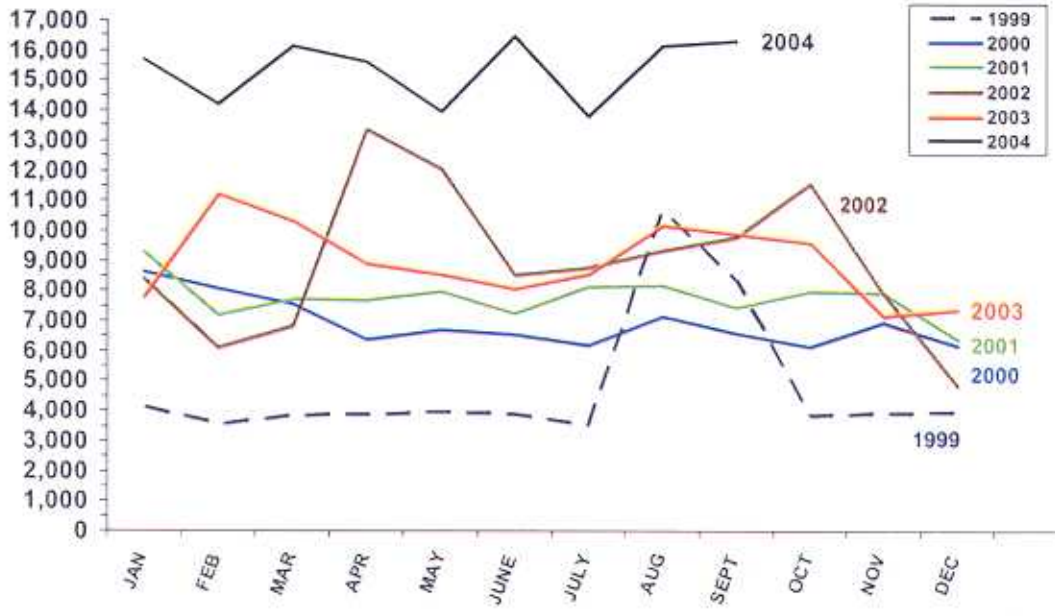
Monthly PA Activity

Calendar Years 2000-2004



Monthly PA Activity

Calendar Years 2000-2004



PRIOR AUTHORIZATION QUARTERLY REPORT
FY00 through FY04
(July 1999 - September 2004)

CALL VOLUME -SEPTEMBER 2004

SEPT 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	904	15	813	62	14	192	413	91	0	208	878	5	1	17	3	889	4	1	1	1	0	7	1
2	796	16	712	35	33	70	480	85	0	161	766	10	3	13	4	788	2	1	5	0	0	0	0
3	788	8	461	54	265	50	534	78	0	126	761	5	4	14	4	782	0	0	0	0	1	5	0
4	172	0	169	2	1	23	95	9	0	45	172	0	0	0	0	171	0	1	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	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7	775	10	483	73	209	88	448	69	0	170	746	7	0	14	8	768	3	1	1	0	0	2	0
8	770	15	688	55	12	175	384	88	0	122	755	4	2	4	5	765	5	0	0	0	0	0	0
9	828	14	717	73	24	178	415	74	0	161	810	10	0	5	3	810	8	1	0	0	0	9	0
10	739	22	633	71	12	212	221	113	0	193	720	6	2	7	4	726	7	0	0	0	0	5	0
11	151	0	138	10	3	33	61	13	0	44	140	1	0	7	3	151	0	0	0	0	0	0	0
12	56	0	53	1	2	6	31	3	0	16	52	0	0	2	2	56	0	0	0	0	0	0	0
13	707	19	603	73	12	180	210	82	0	235	684	3	3	11	6	696	1	2	0	0	0	8	0
14	775	31	637	66	41	184	213	135	0	243	722	19	4	17	13	760	5	2	0	0	0	8	0
15	711	20	605	65	21	181	245	108	0	177	683	8	0	18	2	697	2	1	0	0	0	11	0
16	688	13	589	59	27	119	305	80	0	184	661	8	1	12	6	675	3	0	1	0	0	8	1
17	678	11	573	77	17	97	287	133	0	161	649	16	1	8	4	646	12	3	2	0	1	14	0
18	156	0	153	2	1	23	83	5	0	45	146	0	0	10	0	155	0	0	0	0	1	0	0
19	43	0	39	3	1	7	23	4	0	9	42	0	0	0	1	43	0	0	0	0	0	0	0
20	700	26	586	68	20	195	227	111	0	167	684	4	2	3	7	675	5	2	1	0	1	15	0
21	737	18	617	63	39	105	350	116	0	166	701	13	7	9	7	710	8	1	1	0	0	17	0
22	730	18	636	61	15	108	332	107	0	181	697	11	0	19	3	696	5	0	2	0	1	26	0
23	767	10	668	74	15	108	417	88	0	154	751	4	3	4	5	745	4	1	0	0	0	16	0
24	661	22	563	64	12	102	306	107	0	146	636	5	1	18	1	631	6	0	0	1	0	24	0
25	174	0	169	4	1	23	96	19	0	36	174	0	0	0	0	174	0	0	0	0	0	0	0
26	41	0	41	0	0	10	22	0	0	9	41	0	0	0	0	41	0	0	0	0	0	0	0
27	695	19	576	86	14	182	230	108	0	172	668	7	0	12	8	674	8	1	0	0	1	10	1
28	702	11	585	79	27	176	262	110	0	154	669	14	1	12	6	684	5	2	0	0	1	9	1
29	767	17	676	63	11	107	415	87	0	157	742	9	0	11	5	747	6	1	0	0	0	13	0
30	662	14	569	54	25	94	299	79	0	190	636	14	1	8	3	645	4	0	0	0	0	13	0
Total	16,373	349	13,752	1,397	874	3,028	7,404	2,102	0	3,832	15,786	183	36	255	113	16,000	103	21	14	2	7	220	4
Percentage	100.00%	2.13%	83.99%	8.53%	5.34%	18.49%	45.22%	12.84%	0.00%	23.40%	96.41%	1.12%	0.22%	1.56%	0.69%	97.72%	0.63%	0.13%	0.09%	0.01%	0.04%	1.34%	0.02%

CALL VOLUME

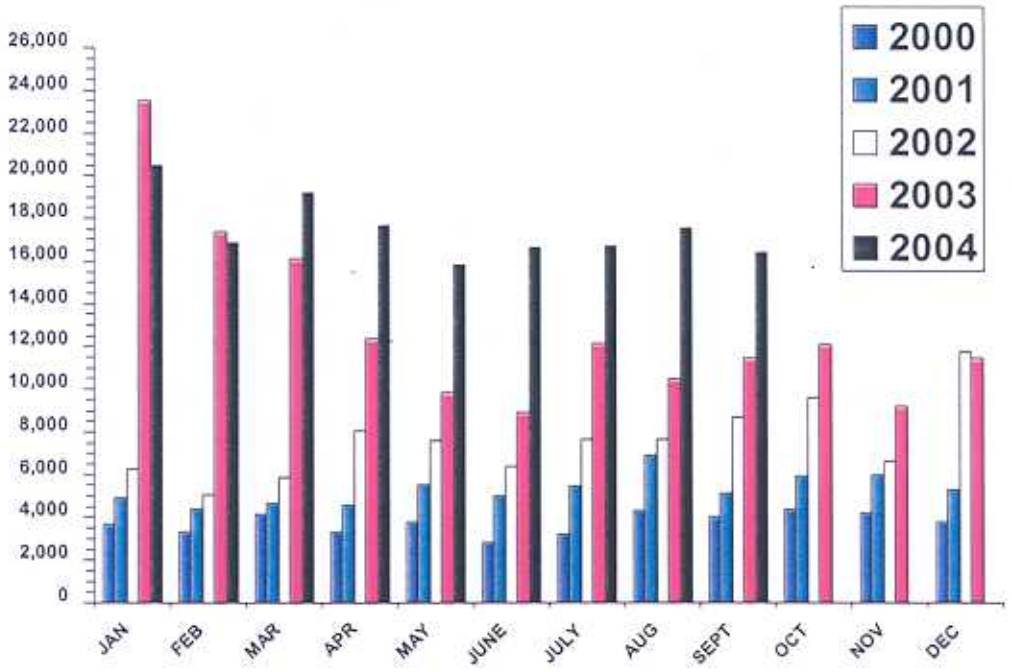
Monthly Totals

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	16,373
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**	**157,307**

* Help Desk Call Center implemented in August 1999.

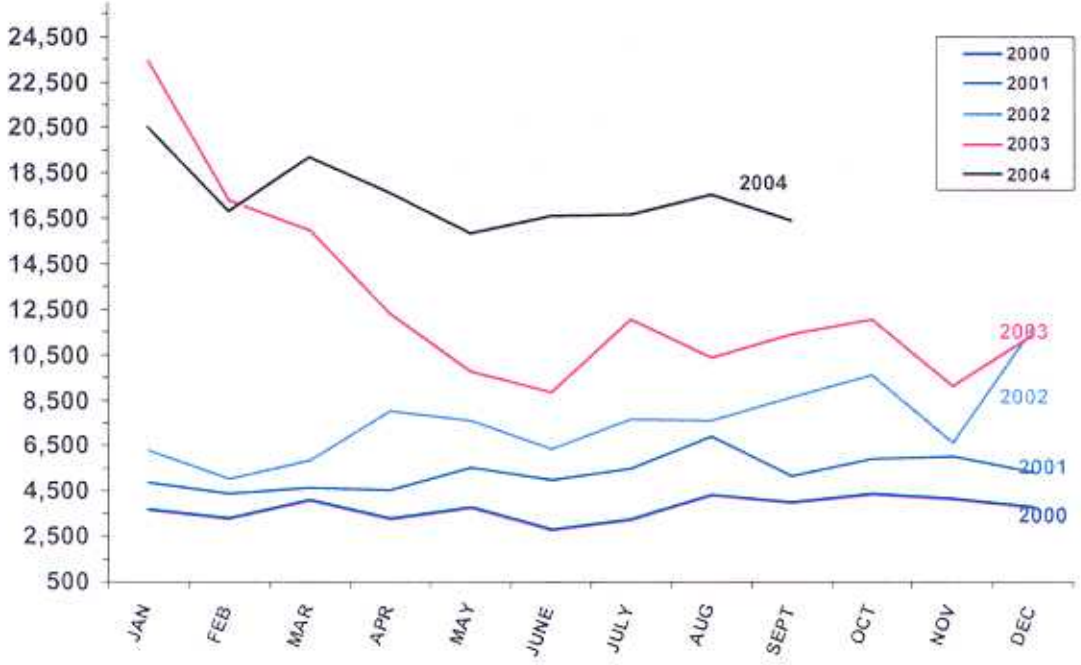
Monthly Call Volume

Calendar Years 2000-2004

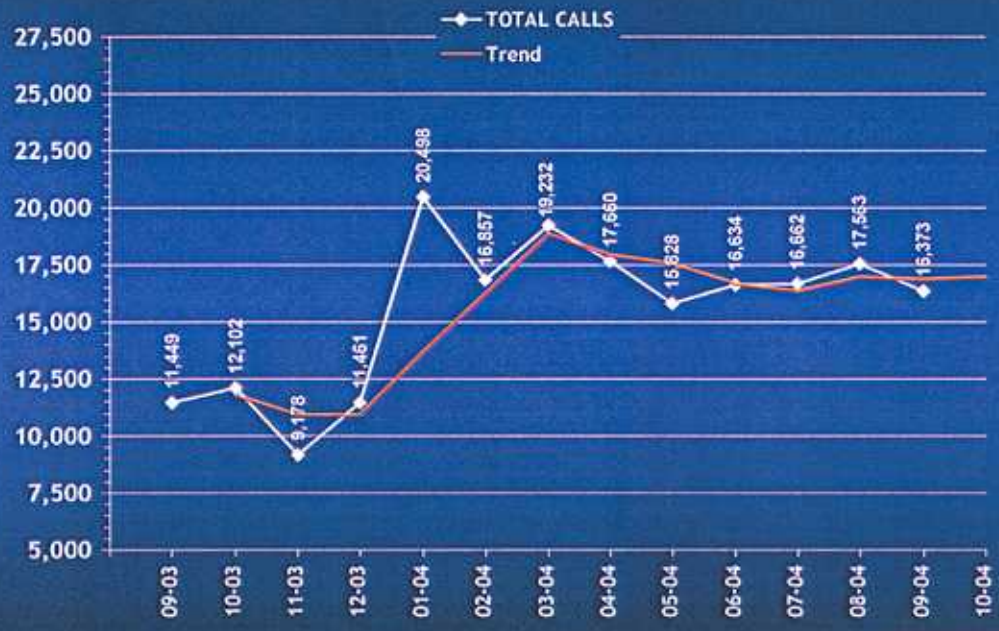


Monthly Call Volume

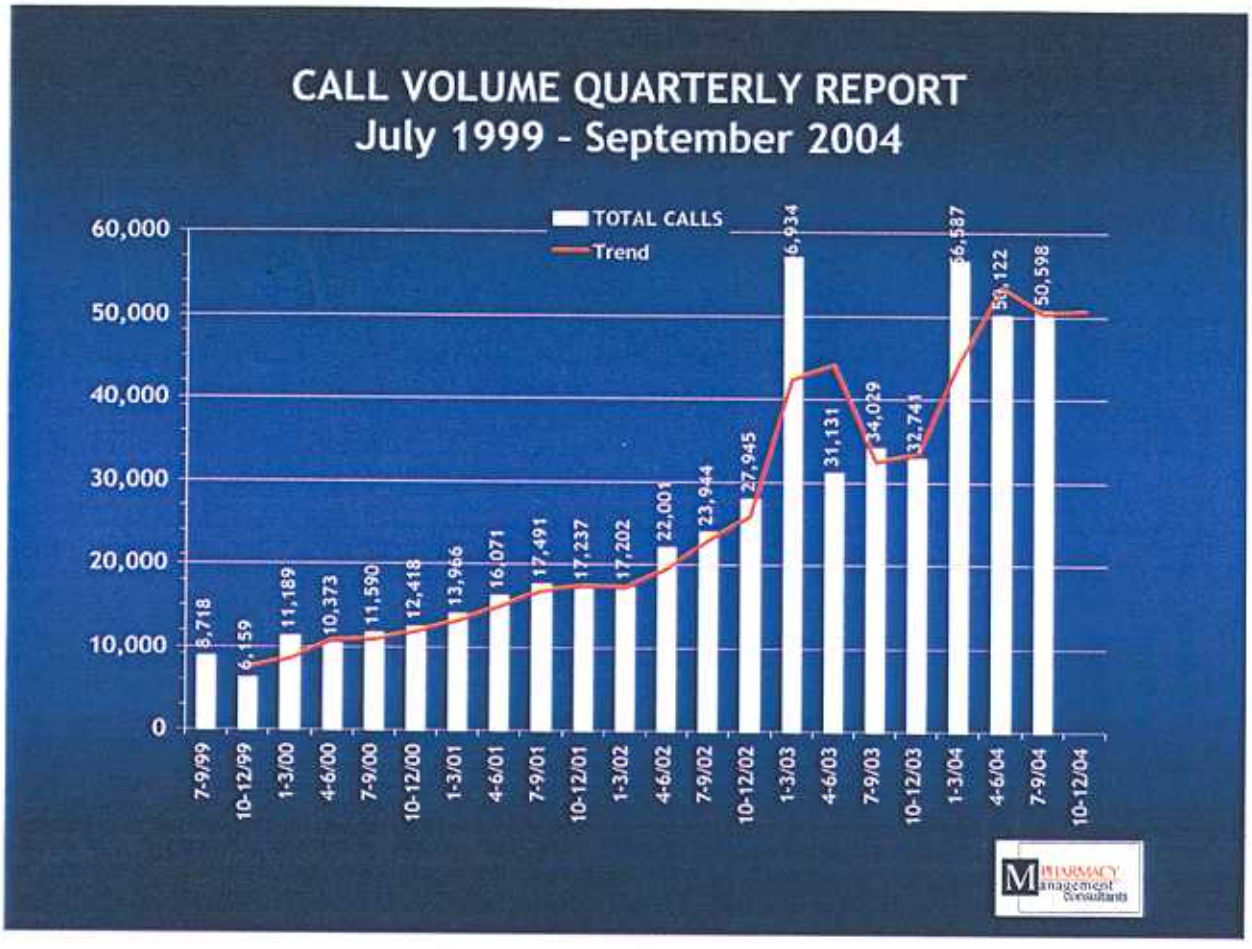
Calendar Years 2000-2004



CALL VOLUME MONTHLY REPORT
September 2003 - September 2004



CALL VOLUME ISSUES
September 2003 - September 2004


CALL VOLUME QUARTERLY REPORT
July 1999 - September 2004
TOTAL CALLS
Trend
60,000
50,000
40,000
30,000
20,000
10,000
0
8,718
6,159
11,189
10,373
11,590
12,418
13,966
16,071
17,491
17,237
17,202
22,001
23,944
27,945
46,934
31,131
34,029
32,741
46,587
50,122
50,598
7-9/99
10-12/99
1-3/00
4-6/00
7-9/00
10-12/00
1-3/01
4-6/01
7-9/01
10-12/01
1-3/02
4-6/02
7-9/02
10-12/02
1-3/03
4-6/03
7-9/03
10-12/03
1-3/04
4-6/04
7-9/04
10-12/04
PHARMACY Management Consultants

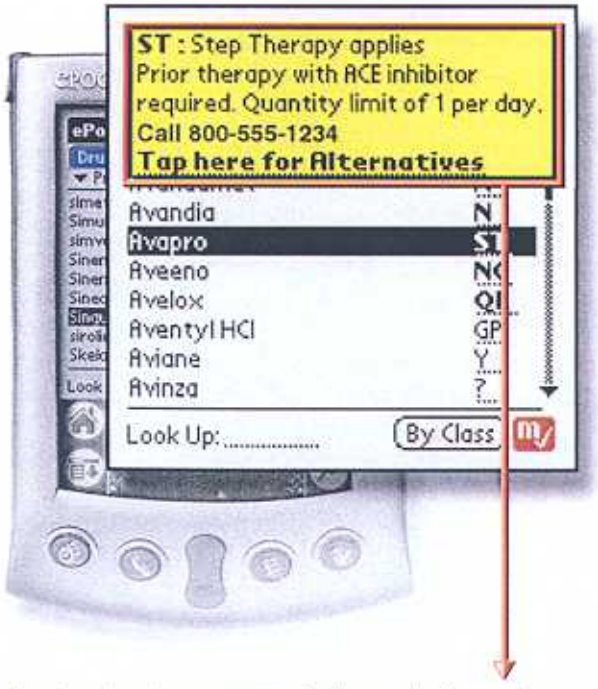
APPENDIX C

Oklahoma Health Care Authority and Epocrates® References

Leading the way to reduce physician hassles and improve quality of care

Epocrates Rx® reviewed in JAMA[1]

"Indispensable," "state of the art" and "the one to have and keep."



Customized pop-up windows deliver drug-specific information, such as benefit design or treatment guidelines.

Epocrates references enable point-of-care access to drug list information

- Verify status and copayment tiers
- View alternatives and generic substitutions
- Look up prior authorization requirements
- Check quantity limits
- Receive drug specific messages directly from Oklahoma Health Care Authority

Epocrates features benefit physicians and members

- Reduce medication errors
- Minimize time dealing with pharmacy call backs
- Improve patient satisfaction
- Monitor drug list updates and changes easily

Over 340,000 healthcare professionals use the Epocrates drug reference guide

- Determine adult and pediatric dosing
- Check for drug interactions
- Guard against adverse reactions and contraindications
- Check pricing information

Access this powerful database easily from your handheld or desktop

- Meet the technical requirements
  - Palm OS or Pocket PC handheld with 3.0 MB of free memory, and/or
  - Personal computer with Internet access
- Download Epocrates handheld software or access Epocrates Rx Online™ from www.epocrates.com
- Select the Oklahoma Medicaid drug list
- AutoUpdate to download the drug list to your handheld
- AutoUpdate frequently to receive updates

www.epocrates.com

OKLAHOMA HEALTH CARE AUTHORITY

[1] JAMA

APPENDIX D

Dementia and Alzheimer's Disease (AD)

Introduction

As our society continues to age, the number of new cases of dementia continues to rise. The prevalence may range from 3 % of those 65 years of age and over to 47 % of those 85 years of age and over[1]. Currently 4.5 million Americans have Alzheimer's disease with a projected 11.3 to 16 million by 2050[2].

Dementia is a group of symptoms characterized by the gradual loss of mental functions including the ability to reason, think, remember, and plan. It may be a primary brain disease or a secondary manifestation of a different disorder. Often considered normal signs of aging, true dementia symptoms are often overlooked. Eventually a person with dementia will lose the ability to perform daily tasks. Changes in behavior and personality may also occur[3].

Several illnesses that cause dementia are: Alzheimer's Disease, Vascular Dementia, Lewy Body Disease, Parkinson's Disease, Pick's Disease, Creutzfeldt-Jakob Disease, and Huntington's Disease.

The most common form of dementia is **Alzheimer's Disease** which occurs in approximately 1 out of every 10 people over the age of 65. Roughly 5 to 10 percent of all AD is genetic in nature and these people may begin to show symptoms of the disease at an earlier age.

The second most common form of dementia is **vascular** in nature and is due to lack of blood or oxygen to the brain. This type of dementia occurs more commonly in men and has a rapid onset and progression.

Lewy Body Disease is most similar to AD and can include symptoms related to movement such as those in Parkinson's Disease.

Parkinson's Disease is caused by loss of neurons which result in dementia. Movements become stiff and shake particularly in the arms and hands. This disease occurs between 50 and 65 years of age in approximately 1 in 1,000 people. Dementia is prevalent in about 20 to 60 % of the people with Parkinson's Disease.

Pick's Disease is caused by cell death in the frontal lobe. This disease occurs most often in 40 to 60 year olds, with initial symptoms of behavior changes, followed by speech loss and ending with dementia.

Creutzfeldt-Jakob Disease is a rare disease caused by an infection of the brain which leads to degeneration. This disease is similar to "mad cow" disease with the infection being caused by prions, a special protein particle. Occurring most often in people over 65, it tends to run in families, and usually follows a quick course leading to death within one year.

Huntington's Disease is caused by cell death and occurs in people 30 to 50 years of age. It is an inherited disease and people usually live for 15 to 20 years after cell death begins. Dementia and movement problems are symptoms of this disease.

Pathophysiology of AD

There are two basic microscopic changes which occur in the brain of an Alzheimer's patient, these changes are thought to be related to the cause, course, and development of the disease.

- Formation of senile plaques composed of β-amyloid polypeptides.
- Neurofibrillary tangles within the neurons composed partly of a protein called tau, which links together forming filaments. Severity of dementia is directly related to the density of these filaments.

The involvement of cholinergic neurons causes the levels of acetylcholine to decline within the synapse along with levels of acetylcholinesterase. Butyrylcholinesterase (another cholinesterase enzyme) increases and also causes a drop in the levels of acetylcholine.

Treatment

There is no drug currently available that will completely protect the neurons from cell death. Acetylcholinesterase inhibitors have been the mainstay of AD treatment and until recently have been the only agents FDA approved for the treatment of the disease. These agents are thought to increase the concentration of acetylcholine through inhibition of its hydrolysis.

In October 2003, memantine (Namenda®) was approved for the treatment of moderate to severe AD. This agent is an N-methyl-D-aspartate (NMDA) receptor agonist. The mechanism of action of memantine is thought to be blockage of pathogenic glutamate activity, while allowing for normal physiological activation of the NMDA receptors (this process is necessary for learning and memory)[4].

- Acetylcholinesterase Inhibitors
  - Donepezil hydrochloride (Aricept®)
  - Rivastigmine tartrate (Exelon®)
  - Galantamine hydrobromide (Reminyl®)
  - Tacrine (Cognex®)
- Memantine hydrochloride (Namenda®)

Other drugs which have been studied, but their use remains controversial, include vitamin E, selegiline, estrogen, anti-inflammatory drugs, and ginkgo biloba.

Cost of Alzheimer's Disease

The average lifetime cost of care for an Alzheimer's patient is $170,000. Approximately 7 out of 10 people with the disease live at home and are cared for by family and friends. The remainder reside in nursing facilities where the average cost for care can range from $42,000 to $70,000 per year. The National direct and indirect costs of caring for an Alzheimer's patient is $100 billion. Medicare costs for AD is expected to rise to $49.3 billion by 2010 and Medicaid costs to $33 billion. Finally, the cost of AD to American businesses is approximately $61 billion a year ($24.6 billion for health care and $36.5 billion for lost productivity, absenteeism, and worker replacement)[2].

Utilization in Oklahoma Medicaid

For the period of July 2003 through June 2004 a total of 5,422 clients had claims for an Anti-Dementia drug paid for through the Medicaid Fee-for-Service Program.

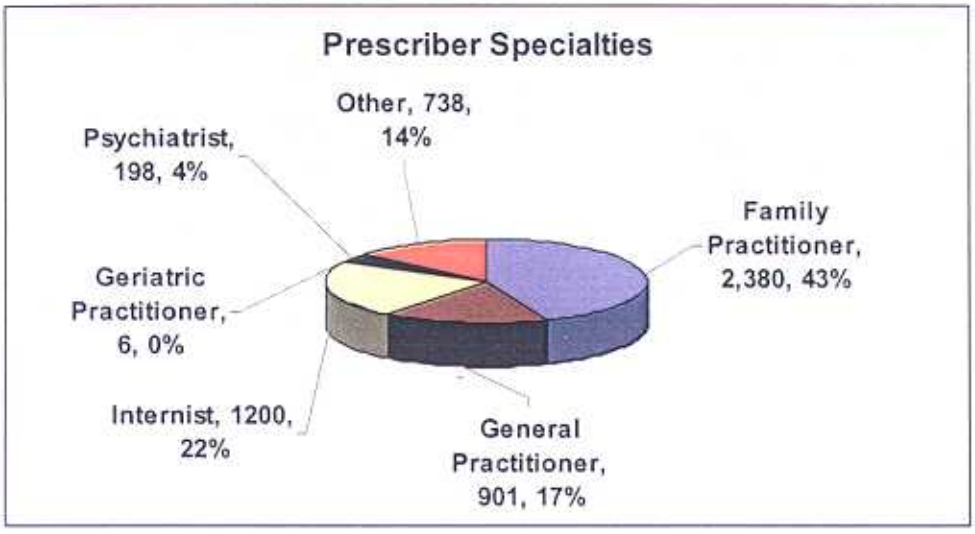
Drugname	Total Claims	Total Units	Total Days	Clients	Total Paid
Aricept 5 mg Tab	5,182	181,788	171,071	1,479	$ 823,192.18
Aricept 10 mg Tab	14,459	462,467	457,046	2,485	$ 2,100,303.23
Reminyl 4 mg Tab	2,379	146,631	69,342	542	$ 345,673.95
Reminyl 8 mg Tab	3,448	201,634	101,508	598	$ 478,966.77
Reminyl 12 mg Tab	426	27,035	13,694	80	$ 64,532.85
Reminyl 4 mg/ml Sol	9	1,400	195	4	$ 2,221.02
Exelon 1.5 mg Cap	1,639	98,464	47,327	443	$ 235,013.35
Exelon 3 mg Cap	2,966	174,373	87,327	585	$ 415,441.88
Exelon 4.5 mg Cap	1,142	68,803	34,749	223	$ 164,918.86
Exelon 6 mg Cap	1,668	97,338	48,796	269	$ 233,506.25
Exelon 2 mg/ml Sol	41	3,960	1,067	7	$ 8,690.28
Namenda 5 mg Tab	488	21,042	11,946	250	$ 43,903.73
Namenda 10 mg Tab	1,373	74,027	38,776	590	$ 153,990.38
Namenda Titration Pak	212	12,701	5,636	191	$ 21,420.11
TOTAL	**35,432**	**1,571,663**	**1,088,480**		**$ 5,091,774.84**

Age and Gender FY04

Age	Female	Male	Total
0 to 9	0	2	2
10 to 19	1	2	3
20 to 34	8	8	16
35 to 49	40	33	73
50 to 64	179	141	320
65 to 79	1,350	517	1,867
80 to 94	2,380	560	2,940
> 95	179	22	201
Total	4,137	1,285	5,422

Cost & Claims by Age FY04

Age	Total Paid	Total Claims
0 to 9	$ 1,751.22	13
10 to 19	$ 1,548.44	8
20 to 34	$ 5,177.45	36
35 to 49	$ 57,184.35	346
50 to 64	$ 278,964.45	1,833
65 to 79	$ 1,729,240.35	11,828
80 to 94	$ 2,822,544.08	19,970
> 95	$ 195,364.50	1,398
Total	$ 5,091,774.84	35,432



Changes to Anti-Dementia Utilization FY04 Compared to FY03

	Fiscal Year 2003	*Fiscal Year 2004*	*Percent Change*
Total Claims	**29,325**	**35,432**	**17.24%**
Aricept	17,168	19,641	12.59%
Reminyl	4,490	6,262	28.30%
Exelon	7,632	7,456	-2.36%
Cognex	35	0	N/A
Namenda	0	2,073	100.00%
Total Cost	**$ 3,771,453.17**	**$ 5,091,774.84**	**25.93%**
Aricept	$ 2,388,148.95	$ 2,923,495.41	18.31%
Reminyl	$ 596,001.44	$ 891,394.59	33.14%
Exelon	$ 782,499.81	$ 1,057,570.62	26.01%
Cognex	$ 4,802.97	$ 0.00	N/A
Namenda	$ 0.00	$ 219,314.22	100.00%
Cost Per Claim	**$ 128.61**	**$ 143.71**	**10.51%**
Aricept	$ 139.10	$ 148.85	6.54%
Reminyl	$ 132.74	$ 142.35	6.75%
Exelon	$ 102.53	$ 141.84	27.72%
Cognex	$ 137.23	$ 0.00	N/A
Namenda	$ 0.00	$ 105.80	100.00%

Comparison of Utilization Pre and Post Inclusion of All Clients in Fee-for-Service Pharmacy Program

	Jan thru Jun 2003	*Jan thru Jun 2004*	*Percent Change*
Total Claims	**14,619**	**19,552**	**25.23%**
Aricept	8,528	10,493	18.73%
Reminyl	2,432	3,371	27.86%
Exelon	3,652	3,615	-1.02%
Cognex	7	0	-100.00%
Namenda	0	2,073	100.00%
Total Cost	**$ 2,078,169.23**	**$ 2,818,089.17**	**26.26%**
Aricept	$ 1,244,085.61	$ 1,590,504.74	21.78%
Reminyl	$ 334,891.06	$ 484,127.21	30.83%
Exelon	$ 498,093.37	$ 524,143.00	4.97%
Cognex	$ 1,099.19	$ 0.00	-100.00%
Namenda	$ 0.00	$ 219,314.22	100.00%
Cost Per Claim	**$ 142.16**	**$ 144.13**	**1.37%**
Aricept	$ 145.88	$ 151.58	3.76%
Reminyl	$ 137.70	$ 143.62	4.12%
Exelon	$ 136.39	$ 144.99	5.93%
Cognex	$ 157.03	$ 0.00	-100.00%
Namenda	$ 0.00	$ 105.80	100.00%

Jan thru Jun 2003

Age	Female	Male	Total
0 to 9	0	0	0
10 to 19	0	0	0
20 to 34	2	5	7
35 to 49	22	20	42
50 to 64	94	73	167
65 to 79	842	325	1,167
80 to 94	1,625	383	2,008
> 95	118	13	131
Total	2,703	819	3,522

Jan thru Jun 2004

Age	Female	Male	Total
0 to 9	0	2	2
10 to 19	1	2	3
20 to 34	4	6	10
35 to 49	32	27	59
50 to 64	154	130	284
65 to 79	1,145	426	1,571
80 to 94	1,998	474	2,472
> 95	149	20	169
Total	3,483	1,087	4,570

Recommendations

The college of pharmacy does not recommend any changes to this category at this time. The college of pharmacy does recommend regular reviews of this category to monitor current trends and practices.

---

[1] Hikal AH, Hikal EM. Dementia in the Elderly. *Drug Topics* 1998(CE):81-83.

[2] Alzheimer's Association. Statistics about Alzheimer's Disease. Available at: <www.alz.org>. Accessed September 20, 2004.

[3] Patient Handout: Dementia. McKesson Health Systems LLC; 2004. Available at: <http:www.home.mdconsult.com>. Accessed September 15, 2004.

[4] Product Monograph: A Guide to Alzheimer's Disease and Namenda®; Forest Pharmaceuticals, Inc., St Louis, Missouri; 2003.

APPENDIX E

Nausea and Vomiting in Pregnancy

Oklahoma Medicaid
October 2004

Introduction

Nausea and vomiting of pregnancy (NVP) is experienced in as much as 70% to 85% of all pregnant women in the United States.[1] Contrary to the notion that the symptoms only occurs in the morning, NVP can occur throughout the day. NVP is generally accepted as an unpleasant, but normal feature of pregnancy, and not a disease as it can be experienced by healthy individuals who give birth to healthy babies. However, there is also a form of excessive, uncontrolled vomiting called Hyperemisis Gravidarum that occurs in less than 1% of pregnancies. This is classified by intractable nausea and vomiting resulting in severe dehydration and metabolic imbalances that requires medical attention. A common criteria used is the presence of acute starvation (indicated by large ketonuria), and approximately 5% loss of prepregnancy weight.[2]

Several theories exist to explain the etiology of NVP. The endocrine etiology theory suggests that certain hormone levels that rise and peak consistently with the onset and duration of symptoms account for the symptoms of NVP.[3,4] The evolutionary adaptation theory proposes that NVP is an adaptation of the mother that have been developed to protect the mother and fetus from foods that might be harmful to either or both during the most sensitive part of fetal development.[5] The last to be mentioned is the psychologic predisposition theory in which it's believed that the NVP is manifested due to a psychological disorder of the mother. However, there have been no controlled studies to support this hypothesis.

Fetal Effects due to Nausea and Vomiting of Pregnancy

NVP is a normal part of a healthy pregnancy, and recent clinical studies have demonstrated that the presence of NVP most often conveys good pregnancy outcomes. The recent meta-analysis involving 18,464 pregnancies found women who've experienced NVP to be significantly less likely to miscarry than women who experienced no symptoms.[6] There have also been studies that show a higher incidence of low birth weight of babies born to mothers that did not experience NVP.[7,8] The thought is not in the symptoms of NVP itself, but rather that NVP serve to ensure the nutritional partitioning favors the fetus as the reduction of energy intake by the mother suppresses maternal tissue synthesis and results in placental weight gain and development of the fetus. Although it is generally accepted that NVP has a positive effect on pregnancy, hyperemesis gravidarum is associated with a higher incidence of low birth weight.[9] However, it is unlikely that hyperemesis gravidarum is associated with an increased risk of fetal malformations.[10]

Decision to Treat Nausea and Vomiting of Pregnancy

NVP is normally limited to early pregnancy, typically peaking around 8-12 weeks and most often resolves spontaneously further into the pregnancy. Since the presence of NVP is associated with positive pregnancy outcomes, there has been no blanket recommendation to treat or eliminate NVP. A decision to treat becomes more apparent in cases of severe NVP affecting the quality of life and productivity of the mother, and is obvious in cases where the well-being of the mother or fetus is at risk as in hyperemesis gravidarum.

A. Non-pharmacologic

1. **Ginger** is found to significantly improve symptoms in NVP and hyperemesis gravidarum.[11]
2. **Acupressure** or electrical stimulation at the P6 or Neguian point on the inside of the wrist has been shown to be of benefit by most studies, but there are some studies that show conflicting results. Methodology and procedure is of concern, however, one study involving electrical stimulation with a commercially available device shows improvement in NVP during the first trimester.[12]
3. **Rest and avoidance of sensory stimuli** that may provoke symptoms are also widely recommended by obstetricians and gynecologists. Avoidance of spicy or fatty foods and other dietary changes are frequently advised, but no trials have yet to evaluate the efficacy of these changes for prevention or treatment of NVP.

B. Pharmacologic

1. **Appendix A**[13] is the recommendations by the American College of Obstetricians and Gynecologists for the treatment of simple NVP to hyperemesis gravidarum.
2. **Appendix B**[14] is a summary of drugs that have been used to treat NVP and their efficacy vs. safety standings.

---

[1] Jewell D, Young G. Interventions for nausea and vomiting in early pregnancy (Cochrane Review). IN: The Cochrane Library, Issue 4, 2003. Chichester, UK: John Wiley & Sons, Ltd. (Meta-analysis.)

[2] Goodwin TM, Montoro M, Mestman JH. Transient hyper-thyroidism and hyperemesis gravidarum: clinical aspects. Am J Obstet Gynecol 1992; 167:648-52.

[3] Yoshimura M, Hershman Jm. Thyrotropic action of human chorionic gonadotropin. Thyroid 1995;5:425-34.

[4] Depue RH, Bernstein L, Ross RK, Judd HL, Henderson BE. Hyperemesis gravidarum in relation to estradiol levels, pregnancy outcome, and other maternal factors; a seroepidemiologoic study. Am J Obstet Gynecol 1987;156:1137-41.

[5] Sherman PW, Flaxman SM. Nausea and vomiting of pregnancy in an evolutionary perspective. Am J Obstet Gynecol 2002; 186:S190-7.

[6] Weigel RM, Weigel MM. Nausea and vomiting of early pregnancy and pregnancy outcome. A meta-analytical review. Br J Obstet Gynaecol 1989;96:1312-8.

[7] Brandes JM. First-trimester nausea and vomiting as related to outcome of pregnancy. Obstet Gynecol 1967;30:427-31.

[8] Tierson FD, Olsen CL, Hook EB. Nausea and Vomiting of pregnancy and association with pregnancy outcome. Am J Obstet Gynecol 1986;155:1017-22.

[9] Chin RK, Lao TT. Low birth weight and hyperemesis gravidarum. Eur J Obstet Gynecol Reprod Biol 1988;28:179-83.

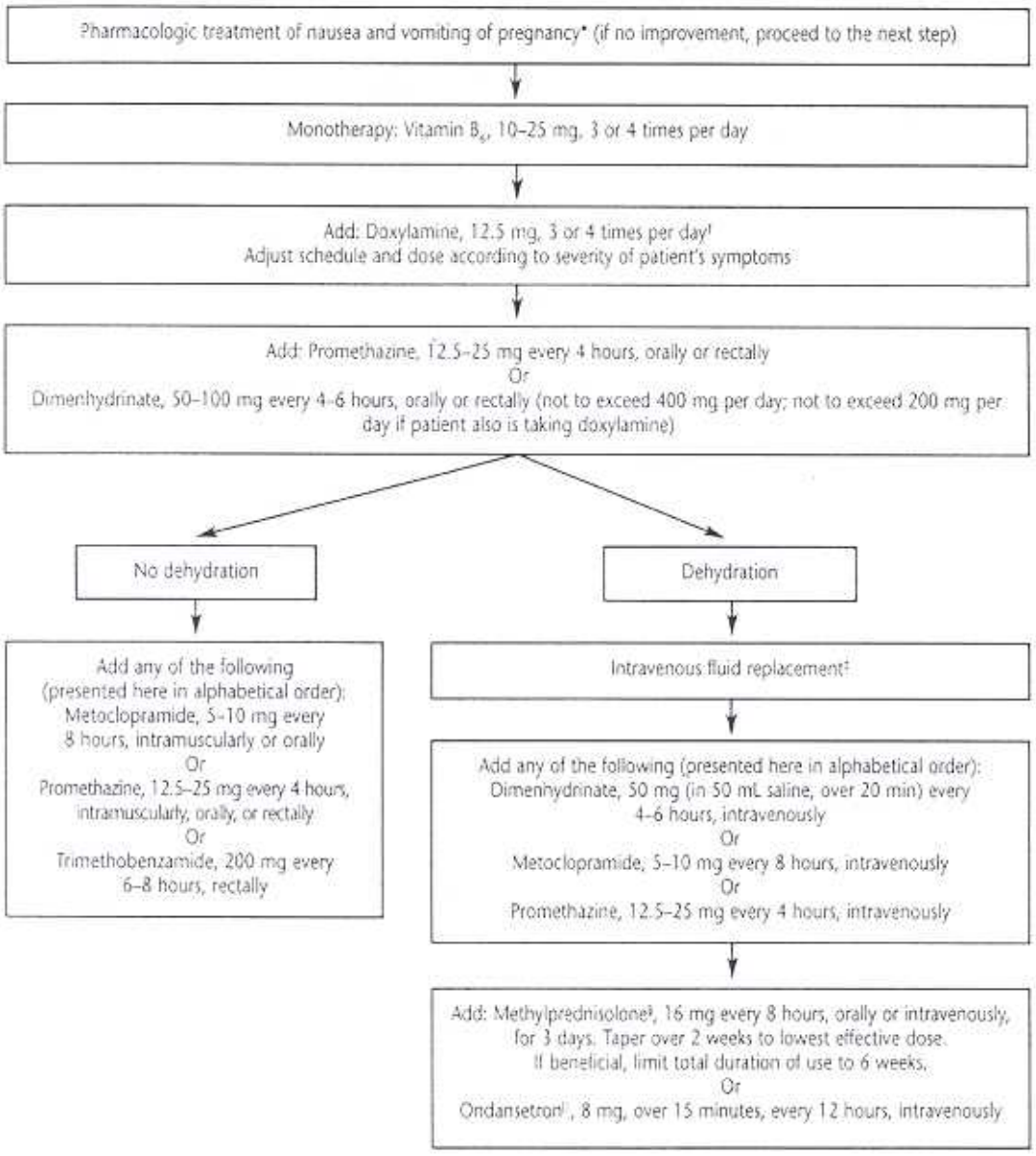
[10] Boneva RS, Moore CA, Botto L, Wong LY, Erickson JD. Nausea during pregnancy and congenital heart defects: a population-based case-control study. Am J Epidemiol 1999;149:717-25.

[11] Vutyavanich T, Kraisarin T, Ruangsri R. Ginger for nausea and vomiting in pregnancy: randomize, double-masked, placebo-controlled trial. Obstet Gynecol 2001;97:577-82.

[12] Rosen T, de Veciana M, Miller HS, Stewart L, Rebarber A, Slotnick RN. A randomized controlled trial of nerve stimulation for relief of nausea and vomiting in pregnancy. Obstet Gynecol 2003;102:129-35.

[13] Nausea and vomiting of pregnancy. ACOG Practice Bulletin No. 52. American College of Obstettricians and Gynecologists. Obstet Gynecol 2004;103:803-15.

[14] Ibid.



*This algorithm assumes other causes of nausea and vomiting have been ruled out. At any step, consider parenteral nutrition if dehydration or persistent weight loss is noted. Alternative therapies may be added at any time during the sequence depending on patient acceptance and clinician familiarity; consider P6 acupressure with wrist bands or acustimulation or ginger capsules, 250 mg 4 times daily.

†In the United States, doxylamine is available as the active ingredient in some over-the-counter sleep aids; one half of a scored 25-mg tablet can be used to provide a 12.5-mg dose of doxylamine.

‡Thiamine, intravenously, 100 mg daily for 2–3 days (followed by intravenous multivitamins), is recommended for every woman who requires intravenous hydration and has vomited for more than 3 weeks. No study has compared different fluid replacements for nausea and vomiting of pregnancy.

§Corticosteroids appear to increase risk for oral clefts in the first 10 weeks of gestation.

¶Safety, particularly in the first trimester of pregnancy, not yet determined; less effect on nausea.

Figure 1. Pharmacologic treatment of nausea and vomiting of pregnancy. (Adapted from Levichek Z, Atanackovic G, Oepkes D, Maltepe C, Einarson A, Magee L, et al. Nausea and vomiting of pregnancy. Evidence-based treatment algorithm. Can Fam Physician 2002;48:267–8, 277.)

Table 1. Summary of Drugs Used to Treat Nausea and Vomiting of Pregnancy

Agent	Randomized Controlled Trial*	Comments on Efficacy	Comments on Safety
H, blockers		Effective in reducing nausea and vomiting of pregnancy	No increased risk of malformations
Doxylamine	√		
Dimenhydrinate	√		
Cetirizine			
Meclizine	√		
Buclizine	√		
Hydroxyzine	√		
Diphenhydramine			
Anticholinergics		No effectiveness trials for nausea and vomiting of pregnancy	No increased risk of malformations
Scopolamine			
Dopamine Antagonists			
Benzamides			
Trimethobenzamide	√	Effective in reducing nausea and vomiting of pregnancy	No known malformations
Metoclopramide		No trials regarding efficacy	No known malformations
Butyrophenones			
Droperidol			One study of limited power identified no known malformations Maternal risk of prolonged Q-T interval
Haloperidol			
Phenothiazines			
Promethazine	√	Effective in reducing nausea and vomiting of pregnancy	Bulk of evidence indicates no teratogenicity (isolated case report† discounted in meta-analysis)
Prochlorperazine			
Chlorpromazine			
Perphenazine			
Benzodiazepines			
Diazepam			
5-Hydroxytryptamine 3 receptor agonists			
Ondansetron	√	One trial found equal effectiveness to promethazine	No malformations noted
Steroids		Pooled results do not suggest benefit in decreasing nausea and vomiting of pregnancy	
Adrenocorticotropic hormone	√		
Corticosteroids	√		Small increased risks of clefts

*The drug has been evaluated in at least 1 randomized, controlled trial.

†Rumeau-Rouquette C, Goujard J, Huel G. Possible teratogenic effect of phenothiazines in human beings. Teratology 1977;15:57–64.

Data from Jewell D, Young G. Interventions for nausea and vomiting in early pregnancy (Cochrane Review). In: The Cochrane Library, Issue 4, 2003. Chichester, UK: John Wiley & Sons, Ltd.; and Magee LA, Mazzotta P, Koren G. Evidence-based view of safety and effectiveness of pharmacologic therapy for nausea and vomiting of pregnancy (NVP). Am J Obstet Gynecol 2002;186:S256–61.

Three recent studies have confirmed an association between oral clefts and methylprednisolone use in the first trimester (73–75). The teratogenic effect is weak, probably accounting for no more than 1 or 2 cases per 1,000 treated women (76). Nevertheless, in view of this probable association, corticosteroid use for hyperemesis gravidarum should be used with caution and avoided before 10 weeks of gestation.

Corticosteroids may be considered as a last resort in patients who will require enteral or parenteral nutrition because of weight loss. The most commonly described regimen is methylprednisolone, 48 mg daily for 3 days, given orally or intravenously. Patients who do not respond within 3 days are not likely to respond, and treatment should be stopped. For those who do respond, the dose may be tapered over a period of 2 weeks.

APPENDIX F

NARCOTIC ANALGESICS – DRUG UTILIZATION REVIEW

Oklahoma Medicaid - October 2004

Drug Category	2002	2,003	$ Change 2002-2003	% Change 2002-2003	1st ½ 2004
Codeine	$5,827.96	$799.51	-$5,028.45	-86.3%	$2,812.00
Codeine/APAP	$297,922.00	$261,561.74	-$36,360.26	-12.2%	$191,469.75
Codeine/ASA	$747.38	$518.49	-$228.89	-30.6%	$395.45
Codeine/Butalbital/ APAP/Caffeine	$26,616.07	$28,716.00	$2,099.93	7.9%	$22,586.35
Codeine/Butalbital/ ASA/Caffeine	$92,583.61	$94,305.97	$1,722.36	1.9%	$52,883.59
Dihydrocodeine/ APAP/Caffeine	$36,787.62	$54,316.86	$17,529.24	47.6%	$37,989.97
Dihydrocodeine/ ASA/Caffeine	$5,133.27	$3,918.65	-$1,214.62	-23.7%	$2,579.63
Fentanyl - Duragesic	$2,524,675.94	$3,455,537.18	$930,861.24	36.9%	$2,759,492.92
Fentanyl - Actiq	$115,809.07	$248,708.85	$132,899.78	114.8%	$315,720.69
Fentanyl - other	$2,005.07	$17.91	-$1,987.16	-99.1%	$0
Hydromorphone	$72,542.78	$94,327.27	$21,784.49	30.0%	$50,979.33
Levorphanol	$0.00	$374.78	$374.78	100.0%	$572.73
Meperidine	$68,596.49	$71,721.64	$3,125.15	4.6%	$47,900.19
Meperidine/ Promethazine	$580.30	$907.54	$327.24	56.4%	$593.12
Methadone	$50,563.02	$73,141.47	$22,578.45	44.7%	$61,564.51
Morphine IR	$168,191.51	$115,916.02	-$52,275.49	-31.1%	$52,711.80
Morphine - MS Contin & generics	$754,552.76	$775,332.12	$20,779.36	2.8%	$467,719.71
Morphine - Kadian	$114,852.51	$183,010.51	$68,158.00	59.3%	$176,034.99
Morphine - Avinza	$63.13	$36,504.81	$36,441.68	57724.8%	$100,736.99
Oxycodone IR	$171,946.39	$193,860.10	$21,913.71	12.7%	$164,361.64
Oxycodone - OxyContin	$3,568,643.23	$4,712,920.51	$1,144,277.28	32.1%	$3,784,573.21
Oxycodone/APAP	$424,875.21	$570,807.68	$145,932.47	34.3%	$548,712.40
Oxycodone/ASA	$16,659.78	$19,945.21	$3,285.43	19.7%	$17,504.20
Oxymorphone	$0.00	$8,478.50	$8,478.50	100.0%	$7,182.75
Propoxyphene	$37,990.12	$49,109.70	$11,119.58	29.3%	$33,130.34
Propoxyphene/ASA/ Caffeine	$10,323.82	$13,042.51	$2,718.69	26.3%	$8,684.62
Propoxyphene/ APAP	$579,070.22	$465,033.92	-$114,036.30	-19.7%	$295,287.24
Sufentanil	$98.00	$841.30	$743.30	758.5%	$200.15
Tramadol	$1,396,904.82	$450,250.97	-$946,653.85	-67.8%	$191,466.00
Tramadol/APAP	$293,854.37	$430,853.01	$136,998.64	46.6%	$332,576.14
Buprenorphine	$293.00	$514.19	$221.19	75.5%	$0.00
Buprenorphine/ Naloxone	$0.00	$71.50	$71.50	100.0%	$269.37
Butorphanol	$153,912.22	$115,402.63	-$38,509.59	-25.0%	$57,109.31
Nalbuphine	$10,442.18	$11,176.42	$734.24	7.0%	$4,836.57
Pentazocine	$1,088.77	$1,038.21	-$50.56	-4.6%	$721.30
Pentazocine/ Naloxone	$96,973.75	$91,269.84	-$5,703.91	-5.9%	$62,991.83

NARCOTIC ANALGESICS – DRUG UTILIZATION REVIEW

Oklahoma Medicaid - October 2004

Drug Category	2002	2,003	$ Change 2002-2003	% Change 2002-2003	1st ½ 2004
Pentazocine/APAP	$17,491.88	$19,000.49	$1,508.61	8.6%	$12,134.81
Hydrocodone/APAP	$2,132,242.27	$2,231,962.35	$99,720.08	4.7%	$1,360,711.17
Hydrocodone/ Ibuprofen	$134,773.48	$120,018.15	-$14,755.33	-10.9%	$88,138.33
Totals	**$13,385,634.00**	**$15,005,234.51**	**$1,619,600.51**	**12.1%**	**$11,315,335.10**

Summary Table:

Year	Claims	Units	Days	Clients	Amount Paid
2002	330,247	21,513,943	4,646,836	81,124	$13,385,634.00
2003	320,127	21,811,137	4,762,310	84,506	$15,005,234.51
% Change 2002 to 2003	**-3.1%**	**1.4%**	**2.5%**	**4.2%**	**12.1%**
1st ½ 2004	277,538	17,347,221	3,807,661	87,981	$11,315,335.14

Year	$/Day	$/Unit	$/Client
2002	$2.88	$0.62	$165.00
2003	$3.15	$0.69	$177.56
% Change 2002 to 2003	**9.4%**	**10.6%**	**7.6%**
1st ½ 2004	$2.97	$0.65	$128.61

Claims by age & gender, 2003:

Age	Female	Male	Total	%
0 to 9	4,366	5,179	9,545	11.3%
10 to 19	9,455	6,325	15,780	18.7%
20 to 34	14,244	1,685	15,929	18.8%
35 to 49	7,849	3,946	11,795	14.0%
50 to 64	7,166	3,510	10,676	12.6%
65 to 79	8,712	3,122	11,834	14.0%
80 to 94	6,856	1,366	8,222	9.7%
95 and over	650	75	725	0.9%
2003 Total	**59,298**	**25,208**	**84,506**	**100.0%**

Claims per client, 2003:

# Of Claims	# Of Clients	% Of Clients
1 to 5	67,649	80
6 to 10	8,439	10
11 to 15	5,032	6
16 to 20	1,700	2
20 +	1,686	2

Recommendations:

- None at this time.

APPENDIX G

Rheumatoid Arthritis

Oklahoma Medicaid
October 2004

Introduction

Rheumatoid arthritis (RA) is an autoimmune disorder of unknown etiology. Other factors that are involved in RA are environmental influences, genetic markers, tumor-necrosis factor-alpha, interleukin-1, interleukin-6, growth factors and inflamed synovium. Classic symptoms include joint swelling and erythema, stiffness, warmth, and pain. Others include limitation in range of motion, fever, weight loss, anemia, fatigue, rheumatoid nodules, vasculitis, pulmonary fibrosis, ocular disease and pericarditis. RA affects women more than men (3:1). It affects 1% of the population which is approximately 2.5 million adult Americans.[1]

Lab Abnormalities

- Normochromic, normocytic anemia – seen in approximately half of the patients
- Elevated ESR (Erythrocyte sedimentation rate) – seen in 85-95% of patients
- WBC in synovial fluid
- RF (Rheumatoid factor) – present in 60-70% of patients
- Elevated C-reactive protein
- Decrease in serum albumin

Goals of Therapy

- Control disease activity
- Alleviate pain
- Maintain function for essential activities of daily living
- Increase quality of life
- Slow rate of joint damage
- Induce complete remission

Nonpharmacologic Management

Includes physical therapy, adequate rest, occupational therapy, patient education, supportive services (i.e. Arthritis Foundation)

Pharmacologic Therapy

1. Salicylates or NSAIDS
2. DMARD (Disease modifying anti-rheumatic drugs)
3. Corticosteroids

Diagnosis

According to the American College of Rheumatology (ACR), the diagnosis of RA requires confirmation of at least four of the following criteria:[2]

1. Morning stiffness lasting at least one hour before maximal improvement, for at least 6 consecutive weeks.
2. Soft tissue swelling or effusion, observed by a physician, in at least three of the following joint areas (right or left): proximal interphalangeal (PIP), metacarpophalangeal (MCP), wrist, elbow, knee, ankle, or metatarsophalangeal (MTP) joints, for at least 6 consecutive weeks.
3. Swelling or effusion, observed by a physician, in the proximal interphalangeal, metacarpophalangeal, or wrist joints, for at least 6 consecutive weeks.
4. Symmetrical (right and left sides) swelling or fluid in the joints mentioned in point 2, observed by a physician, for at least 6 consecutive weeks.
5. Subcutaneous nodules over bony prominences or extensor surfaces, or in juxta-articular regions, observed by a physician.
6. Demonstration of serum rheumatoid factor (RF) detected by any method that has been positive in less than 5% of control subjects.
7. Radiographic evidence in the hands or wrists of articular erosions or osteopenia in or around the affected joints

Table of Available DMARDs

Generic (Brand)	Onset (Months)	Dosing	Adverse Effects	Monitoring Parameters
More Commonly Used DMARDs				
Hydroxychloroquine (Plaquenil)	2-6	200-40 mg/day; max= 6.5 mg/kg/day	Nausea, HA, ocular toxicity, myopathy	Eye exam, CBC, LFTs
Sulfasalazine (Azulfidine)	1-3	500 mg/day; max= 3000 mg/day	Dizziness, nausea, diarrhea, HA, rash, abnormal LFTs	CBC, LFTs, SCr
Methotrexate (Rheumatrex)	1-2	5-20 mg/week	Nausea, diarrhea, mouth ulcers, rash, alopecia, abnormal LFTs, renal failure, leukopenia, myelsuppression	LFTs, SCr, CBC, chest x-ray
Less Frequently Used DMARDs				
Auranofin (Ridaura)	4-6	3-6 mg/day; max= 9 mg/day	Itching, rash, stomatitis, conjunctivitis, proteinuria	SCr (avoid if CrCl <50ml/min), u/a, CBC
Azathioprine (Imuran)	2-3	50-150 mg/day	Chills, fever, N/V, diarrhea, leucopenia, thrombocytopenia	CBC, LFTs
Cyclosporine (Neoral)	2-4	3-10 mg/kg/day	HTN, HA, nausea, parasthesia, tremor, HA, leukopenia	BP, SCr, LFTs, serum drug levels
Gold Salts (IM) (Aurolate)	3-6	25-50mg IM q 2-4 weeks	Itching, rash, conjunctivitis, stomatitis, proteinuria	CBC w/ diff, renal fx, urinalysis
D-Pennicillamine (Cuprimine)	3-6	250-750 mg/day	Nausea, loss of taste, arthralgia, thrombocytopenia	u/a, CBC, LFTs
Newer DMARDs				
Leflunamide (Arava)	1-4	100 mg/day PO x 3 days (loading dose), then 20 mg/day	Diarrhea, RTI, nausea, rash, HTN, alopecia	LFTs, Scr, BP, eye exam
Etanercept (Enbrel)	0.25-3	25 mg SQ twice a week	HA, injection site reaction, infection, abdominal pain, weakness	s/sx of infection
Infliximab (Remicade)	0.25-4	3 mg/kg IV at 0,2, and 6, and then every 8 weeks	HA, fatigue, fever, nausea, abdominal pain, RTI	s/sx of infection
Anakinra (Kineret)	0.25-1	100 mg/day SQ	HA, injection site reaction, infections	Neutrophil counts
Adalimumab (Humira)	0.25-1	40 mg SC every other week; may increase to 40 mg SC q week in patients not receiving concomitant methotrexate	HA, rash, antibodies, RTI, injection site reaction	anti-adalimumab antibodies(ELISA), anti-dsDNA antibody, CBC

HA = headache; CBC= complete blood count; LFTs= liver function tests; SCr= serum creatinine; CrCl= creatinine clearance; N/V= nausea and vomiting; u/a= urinalysis; s/sx= signs and symptoms; BP= blood pressure; RTI= respiratory tract infection; fx= function; HTN= Hypertension.
Adapted from Comprehensive Pharmacy Review[3]

Trend in DMARDs Utilization

	Fiscal Year 2003	*Fiscal Year 2004*	*Percent Change*
Total Claims	**7,798**	**8,306**	**6.12%**
Plaquenil	2084	2386	12.66%
Azulfidine	1103	1126	2.04%
Rheumatrex	13	5	-160%
Ridaura	62	48	-29.17%
Gold salts	8	2	-300%
Imuran	1301	1146	-13.53%
Neoral	1377	1076	-27.97%
Cuprimine	51	39	-30%
Arava	668	587	-13.8%
Enbrel	752	1264	40.51%
Remicade	4	24	83.33%
Remicade OP	147	57	-157.89%
Kineret	165	138	19.57%
Humira	63	408	84.56%

	Fiscal Year 2003	*Fiscal Year 2004*	*Percent Change*
Total Cost	**$2,387,7317.13**	**$3,421,165.18**	**30.22%**
Plaquenil	$53,672.03	$49,961.74	-7.43%
Azulfidine	$27,111.80	$25,115.85	-7.95%
Rheumatrex	$571.09	$91.55	-523%
Ridaura	$10,833.49	$9,155.79	-18.32%
Gold salts	$228.05	$267.59	14.78%
Imuran	$98,894.61	$73,653.13	-34.27%
Neoral	$446,151.99	$350,626.75	-27.24%
Cuprimine	$4,035.13	$3,913.19	-3.12%
Arava	$219,732.31	$274,659.65	20%
Enbrel	$874,557.21	$1,587,017.76	44.82%
Remicade	$24,359.27	$50,908.98	52.15%
Remicade OP	$339,892.99	$182,676.44	-86.06%
Kineret	$202,304.95	$169,449.76	-19.39%
Humira	$84,972.21	$64,3667	86.8%

	Fiscal Year 2003	Fiscal Year 2004	Percent Change
Cost Per Claim	**$306.23**	**$411.89**	**25.65%**
Plaquenil	$25.75	$20.94	-22.97%
Azulfidine	$24.58	$22.31	-10.17%
Rheumatrex	$43.93	$18.31	-139.92%
Ridaura	$174.73	$190.75	8.40%
Gold salts	$28.51	$97.98	70.90%
Imuran	$76.01	$64.27	-18.26%
Neoral	$324	$325.86	0.57%
Cuprimine	$79.12	$100.34	21.15%
Arava	$328.94	$467.90	29.70%
Enbrel	$1162.97	$1255.55	7.73%
Remicade	$6089.82	$2120.21	-187.23%
Remicade OP	$2312.19	$3204.85	27.85%
Kineret	$1226.09	$1227.90	0.15%
Humira	$1348.77	$1577.62	14.51%

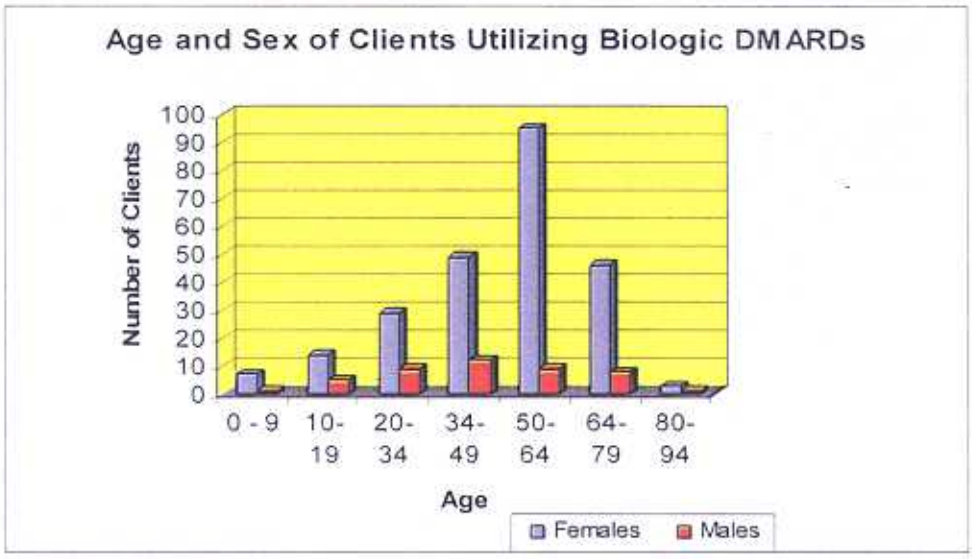
Comparison of Biologic DMARDs

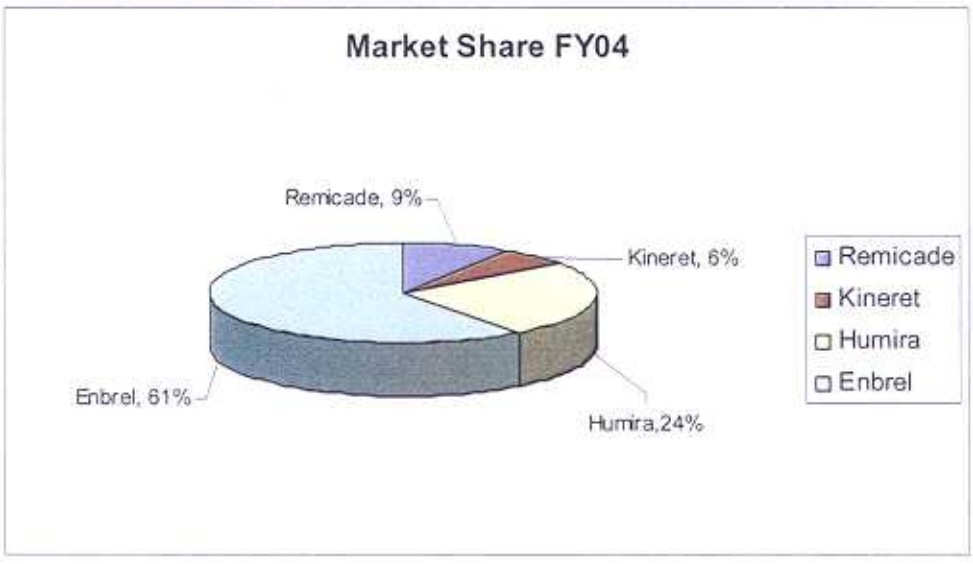
FY03

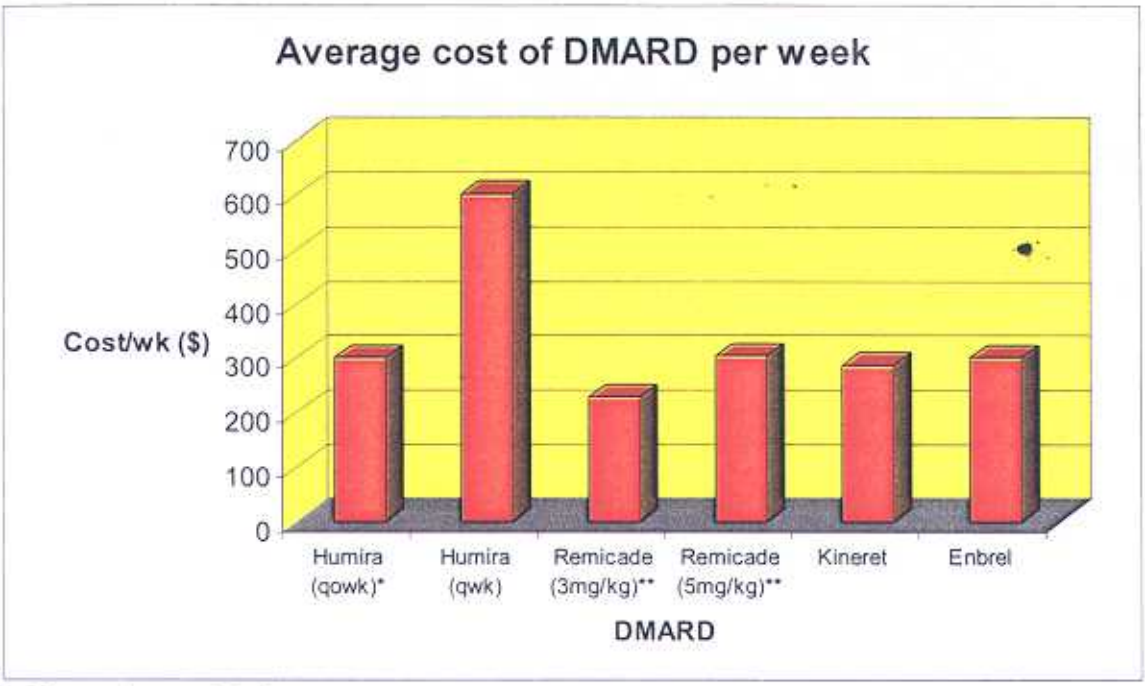
Drug	Clients	Claims	Cost ($)	Cost/Claim ($)	Claim/Client	Days/Claim	Units/Day
Enbrel	179	752	874,557.21	1162.97	5	28	0.3
Remicade (P)	1	4	24,359.27	6089.82	4	1	1.6
Remicade (OP)	28	147	339,892.99	2,312.19	6	N/A	N/A
Kineret	48	165	202,304.95	1,226.09	4	30	1.2
Humira	23	63	84,972.21	1,348.77	3	27	0.06

FY04

Drug	Clients	Claims	Cost ($)	Cost/Claim ($)	Claim/Client	Days/Claim	Units/Day
Enbrel	191	1,264	1,587,017.76	1255.55	7	28	0.30
Remicade (P)	11	24	50,908.98	2120.21	3	16	0.96
Remicade (OP)	19	57	182,676.44	3204.85	3	N/A	N/A
Kineret	19	138	169,449.76	1227.90	8	29	0.82
Humira	82	408	643,667	1577.62	5	28	0.10


Age and Sex of Clients Utilizing Biologic DMARDs
Number of Clients
100
90
80
70
60
50
40
30
20
10
0
0 - 9
10-19
20-34
34-49
50-64
64-79
80-94
Age
Females
Males


Market Share FY04
Remicade, 9%
Kineret, 6%
Humira,24%
Enbrel, 61%
Remicade
Kineret
Humira
Enbrel



* = Every other week dosing
** = Based on a 70kg (154lb) person and rounding up to next whole vial

Management of Rheumatoid Arthritis (Guidelines based on ACR 2002 update)[4]

- Establish diagnosis early
- Document baseline disease activity
- Estimate prognosis
- Initiate therapy
  - Begin patient education
  - Start DMARD therapy within 3 months
  - Consider NSAID
  - Consider local or low-dose systemic corticosteroid
  - Start physical/occupational therapy
- If inadequate response (ongoing active disease after 3 months of maximal therapy), then:
  - Change or add DMARD
  - If no previous MTX treatment:
    - Start MTX or
    - Other monotherapy or
    - Combination therapy
  - If suboptimal response to MTX:
    - Combination therapy or
    - Other monotherapy or

- Biologic DMARDS (either monotherapy or combination)
- If failure of DMARDS and patient has symptomatic or structural joint damage, then consider surgery.

New First Line Regimen Approved

On September 30, 2004 the FDA approved an expanded label for REMICADE® (infliximab) in combination with methotrexate, as a first line regimen to treat patients with moderate to severe RA. The expanded label eliminates the requirement that patients must fail to respond to methotrexate, the current standard of treatment for RA, before starting on the REMICADE regimen. [5]

Active Controlled Study of Patients Receiving Infliximab for Treatment of Rheumatoid Arthritis of Early Onset: The ASPIRE Trial [6]

- Design: randomized, double blind, active control study
- Setting: 125 centers in North America and Europe
- Duration: 54 weeks
- Participants: 1,049 patients with early RA (<3year duration) randomized to received methotrexate and either placebo, 3mg/kg of REMICADE or 6mg/kg of REMICADE at weeks 0, 2 and 6 and then every eight weeks thereafter
- Primary endpoints: improvement of signs and symptoms, progression of structural damage and improvement in physical function
- Results: The mean change from baseline in erosion score for the combined REMICADE group at week 54 was –0.75 (improvement), whereas the mean change for the placebo group was 3.57 (worsening) ($p<0.001$).

Recommendation

With Remicade recently being approved as a first line agent with Methotrexate and looking at the average cost per week of each DMARD (which are approximately equivalent), the college of pharmacy recommends continued monitoring at this time.

References:

[1] American College of Rheumatology. Available on the internet at: http://www.rheumatology.org/public/factsheets/ra.asp?aud=stu

[2] O'Dell JR. Drug Therapy: Therapeutic Strategies for Rheumatoid Arthritis. N Engl J Med. 350(25):2591-2602, 2004 June 17.

[3] Shargel: Comprehensive Pharmacy Review., 5th ed. Copyright © 2004 Lippincott Williams and Wilkins

[4] American College of Rheumatology. Arthritis and Rheumatism. 46(2): 328-346, 2002 February

[5 & 6] P&T Committee. Available on the internet at: http://www.ptcommunity.com/Daily/DailyDetail.cfm?chosen=56961

APPENDIX H

FDA News

FOR IMMEDIATE RELEASE
P04-95
September 30, 2004

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

FDA Issues Public Health Advisory on Vioxx as its Manufacturer Voluntarily Withdraws the Product

The Food and Drug Administration (FDA) today acknowledged the voluntary withdrawal from the market of Vioxx (chemical name rofecoxib), a non-steroidal anti-inflammatory drug (NSAID) manufactured by Merck & Co. FDA today also issued a Public Health Advisory to inform patients of this action and to advise them to consult with a physician about alternative medications.

Merck is withdrawing Vioxx from the market after the data safety monitoring board overseeing a long-term study of the drug recommended that the study be halted because of an increased risk of serious cardiovascular events, including heart attacks and strokes, among study patients taking Vioxx compared to patients receiving placebo. The study was being done in patients at risk of developing recurrent colon polyps.

"Merck did the right thing by promptly reporting these findings to FDA and voluntarily withdrawing the product from the market," said Acting FDA Commissioner Dr. Lester M. Crawford. "Although the risk that an individual patient would have a heart attack or stroke related to Vioxx is very small, the study that was halted suggests that, overall, patients taking the drug chronically face twice the risk of a heart attack compared to patients receiving a placebo."

Dr. Crawford added that FDA will closely monitor other drugs in this class for similar side effects. "All of the NSAID drugs have risks when taken chronically, especially of gastrointestinal bleeding, but also liver and kidney toxicity. They should only be used continuously under the supervision of a physician."

FDA approved Vioxx in 1999 for the reduction of pain and inflammation caused by osteoarthritis, as well as for acute pain in adults and for the treatment of menstrual pain. It was the second of a new kind of NSAID (Cox-2 selective) approved by FDA. Subsequently, FDA approved Vioxx to treat the signs and symptoms of rheumatoid arthritis in adults and children.

At the time that Vioxx and other Cox-2 selective NSAIDs were approved, it was hoped that they would have a lower risk of gastrointestinal ulcers and bleeding than other NSAIDs (such as ibuprofen and naproxen). Vioxx is the only NSAID demonstrated to have a lower rate of these side effects.

Merck contacted FDA on September 27, 2004, to request a meeting and to advise the agency that the long-term study of Vioxx in patients at increased risk of colon polyps had been halted. Merck and FDA officials met the next day, September 28, and during that meeting the company informed FDA of its decision to remove Vioxx from the market voluntarily.

In June 2000, Merck submitted to FDA a safety study called VIGOR (Vioxx Gastrointestinal Outcomes Research) that found an increased risk of serious cardiovascular events, including heart attacks and strokes, in patients taking Vioxx compared to patients taking naproxen. After reviewing the results of the VIGOR study and other available data from controlled clinical trials, FDA consulted with its Arthritis Advisory Committee in February 2001 regarding the clinical interpretation of this new safety information. In April 2002, FDA implemented labeling changes to reflect the findings from the VIGOR study. The labeling changes included information about the increase in risk of cardiovascular events, including heart attack and stroke.

Recently other studies in patients taking Vioxx have also suggested an increased risk of cardiovascular events. FDA was in the process of carefully reviewing these results, to determine whether further labeling changes were warranted, when Merck informed the agency of the results of the new trial and its decision to withdraw Vioxx from the market.

Additional information about this withdrawal of Vioxx, as well as questions and answers for patients, is available online at http://www.fda.gov/cder/drug/infopage/vioxx/default.htm.

####

FDA Public Health Advisory
Questions and Answers
Merck & Co. Press Release

Drug Abuse Warning Network

The DAWN Report

JULY 2004

Oxycodone, Hydrocodone, and Polydrug Use, 2002

In Brief

In recent years, the abuse of opioid pain relievers[1] has been recognized as a serious and growing public health problem.[2,3] Recent estimates from the Drug Abuse Warning Network (DAWN) showed that drug abuse-related emergency department (ED) visits involving opioid pain relievers have been increasing since 1994. Two of these pain relievers, oxycodone and hydrocodone,[4] account for a substantial proportion of the increase (Figure 1).

- In 2002, opioid pain relievers accounted for more than 119,000 ED mentions, or 10 percent of all the drug mentions in drug abuse-related ED visits. Oxycodone and hydrocodone were the most frequently named pain relievers, accounting for 40 percent (47,594 mentions) of the opioid pain relievers involved in these ED visits.
- Approximately three-quarters of ED visits involving oxycodone and hydrocodone involved additional drugs (71% and 78%, respectively), while only 54 percent of all drug abuse-related visits involved multiple drugs.
- The most frequent substances found in combination with oxycodone and hydrocodone in drug abuse-related ED visits were alcohol, benzodiazepines, other opioid pain relievers, and cocaine.

Introduction

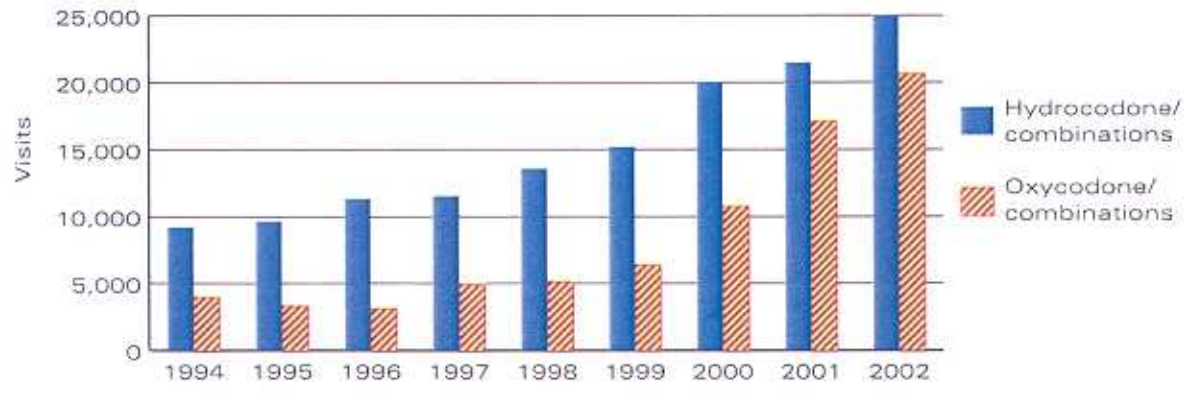
In recent years, the abuse of opioid pain relievers has been recognized as a serious and growing public health problem.[5]

DAWN is a national public health surveillance system that monitors drug abuse-related ED visits. It collects data on all drugs involved in such visits and is useful for tracking trends in the consequences of drug abuse involving drugs such as opioid pain relievers.

This report focuses on drug abuse-related ED visits involving 2 frequently reported opioid pain relievers—oxycodone and hydrocodone. These drugs are marketed under many brand names, including Vicodin®, OxyContin®, and Percocet®. Some formulations contain a single active ingredient (e.g., OxyContin®

FIGURE 1

Trends in drug abuse-related ED visits involving hydrocodone and oxycodone, coterminous U.S., 1994-2002



SOURCE: Office of Applied Studies, SAMHSA, Drug Abuse Warning Network, 2002 (03/2003 update)

contains only oxycodone), while others contain the opioid in combination with acetaminophen, aspirin, or ibuprofen (e.g., Vicodin® contains both hydrocodone and acetaminophen). ED visits involving both single-ingredient and combination formulations are included in this analysis.

Opioid Pain Relievers in ED Visits Related to Drug Abuse

In 2002, opioid pain relievers accounted for more than 119,000 ED mentions,[6] or 10 percent of all drug mentions in drug abuse-related ED visits. Opioid pain relievers were as frequent as heroin or marijuana in ED visits related to drug abuse, but less frequent than cocaine or alcohol.

More than one-third (35%) of ED mentions of opioid pain relievers were not identified by name (Figure 2). Of those that were named, oxycodone (19% of opioid pain reliever mentions) and hydrocodone (21%) were the most frequent. Other opioid pain relievers, such as morphine, occurred much less frequently.

Trends in Oxycodone and Hydrocodone in ED Visits: 1994-2002

Between 1994 and 2002, mentions of oxycodone and hydrocodone increased in ED visits related to drug abuse (Figure 1).

In 1994, ED mentions of oxycodone numbered about 4,000 nationally. By 2002, ED mentions of oxycodone had increased to more than 22,000 mentions—an increase of 450 percent.

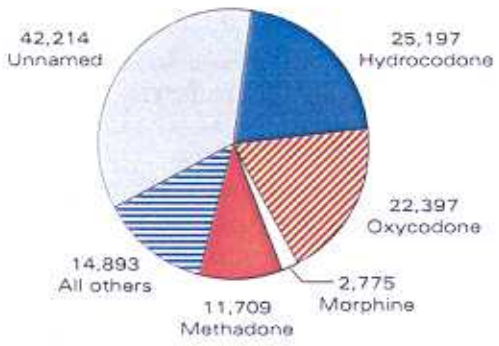
In 1994, ED mentions of hydrocodone were more than twice as frequent as oxycodone, but that gap has narrowed. By 2002, ED mentions of hydrocodone had risen by 170 percent, from about 9,300 in 1994 to more than 25,000 in 2002.

Polydrug Use

In 2002, more than half (54%) of drug abuse-related ED visits involved multiple drugs. Over a third (36%) involved 2 drugs; 13 percent involved 3 drugs; and the remaining 6 percent involved 4 or 5 drugs. Alcohol was involved in nearly a third (31%) of drug abuse-related ED visits.

FIGURE 2

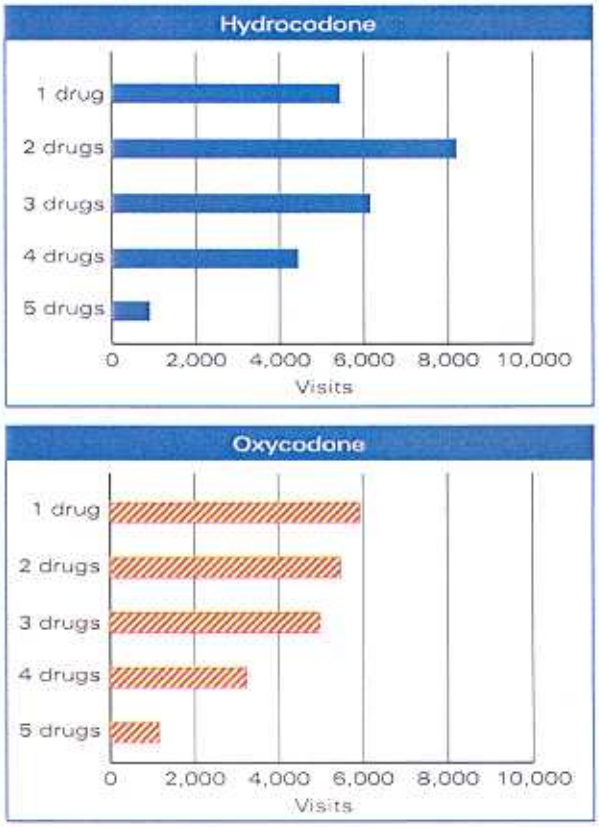
Mentions of opioid pain relievers, by specific drug, 2002



SOURCE: Office of Applied Studies, SAMHSA, Drug Abuse Warning Network, 2002 (03/2003 update).

FIGURE 3

Number of drugs involved in oxycodone- and hydrocodone-related ED visits: 2002



SOURCE: Office of Applied Studies, SAMHSA, Drug Abuse Warning Network, 2002 (03/2003 update).

Polydrug use was even more prevalent among the ED visits involving oxycodone and hydrocodone. In 2002, 71 percent of oxycodone-related ED visits and 78 percent of hydrocodone-related ED visits involved multiple drugs.

However, oxycodone and hydrocodone appeared to have different polydrug patterns (Figure 3). For oxycodone, single-drug visits were the most frequent (29% of 20,748 visits), with 2- or 3-drug visits occurring in similar numbers (between 5,000 and 6,000 visits). For hydrocodone, 2-drug visits were most frequent (33% of 25,109 visits), with fewer visits involving 3 or 4 drugs. The numbers of 5-drug visits were similar for oxycodone and hydrocodone (6% and 4%, respectively).

Drugs Used in Combination With Oxycodone and Hydrocodone

More than 200 different drugs were reported to DAWN in combination with oxycodone and hydrocodone. Major substances of abuse, benzodiazepines,[7] other opioid pain relievers, and a muscle relaxant were the most frequent co-occurring drugs in oxycodone- and hydrocodone-related ED visits (Table 1).

More than 40 percent of oxycodone- and hydrocodone-related ED visits also involved a major substance of abuse. Alcohol was the most frequent of these, followed by cocaine, heroin, and marijuana. About one-fifth of oxycodone visits and a quarter of hydrocodone visits also involved a benzodiazepine. The most frequent benzodiazepines were alprazolam, diazepam, and clonazepam.

More than 3,500 ED visits involving oxycodone or hydrocodone also involved another opioid pain reliever. About 3,000 of these visits involved both oxycodone and hydrocodone. Among the other opioid pain relievers, methadone appeared in about 5 percent of visits involving oxycodone.

Carisoprodol, which is used therapeutically as a muscle relaxant, was present in 4 percent of ED visits involving oxycodone and in 8 percent of ED visits involving hydrocodone.

TABLE 1

Drugs in combination with oxycodone and hydrocodone, drug abuse-related ED visits, 2002

	Oxycodone		Hydrocodone	
Total visits	20,748	(100%)	25,109	(100%)
Number of drugs in visit				
Single-drug visits	5,918	(29%)	5,439	(22%)
Multiple-drug visits	14,830	(71%)	19,671	(78%)
2 drugs	5,462	(26%)	8,191	(33%)
3 drugs	4,980	(24%)	6,147	(24%)
4 drugs	3,229	(16%)	4,432	(18%)
5 drugs	1,158	(6%)	901	(4%)
Drugs in combinations				
Other opioid analgesic	3,785	(18%)	3,562	(14%)
oxycodone			3,049	(12%)
hydrocodone	3,049	(15%)		
Major substances of abuse	9,128	(44%)	10,735	(43%)
alcohol	6,893	(33%)	7,864	(31%)
cocaine	2,393	(12%)	2,269	(9%)
heroin	1,614	(8%)	961	(4%)
marijuana	1,545	(7%)	1,290	(5%)
Benzodiazepines	4,296	(21%)	6,424	(26%)
alprazolam	1,516	(7%)	3,041	(12%)
diazepam	1,277	(6%)	1,628	(7%)
clonazepam	880	(4%)	941	(4%)
unnamed benzodiazepine	486	(2%)	559	(2%)
lorazepam	450	(2%)	605	(2%)

SOURCE: Office of Applied Studies, SAMHSA, Drug Abuse Warning Network, 2002 (03/2003 update).

The DAWN Report is published periodically by the Office of Applied Studies, Substance Abuse and Mental Health Services Administration (SAMHSA). This issue was written by Dr. Judy Ball and Dana Lehder Roberts (OAS/SAMHSA).

End Notes

[1] Opioid pain relievers are synthetic medications with effects similar to substances derived from opium. This publication focuses on 2: oxycodone and hydrocodone.

[2] The Substance Abuse and Mental Health Services Administration (SAMHSA) has launched an educational campaign to combat prescription drug misuse and abuse. For more information, go to http://www.rx.samhsa.gov/.

[3] For information on the prevalence of prescription drug misuse nationally, see Substance Abuse and Mental Health Services Administration, Office of Applied Studies. *The NHSDA Report: Nonmedical Use of Prescription-Type Drugs among Youths and Young Adults.* Rockville, MD. January 16, 2003. http://www.oas.samhsa.gov/2k3/prescription/prescription.cfm.

[4] DAWN refers to each drug in terms of its generic name, as drugs are available under many different brand names.

[5] On August 6, 2003, the 108th Congress convened a hearing before the Senate Committee on Governmental Affairs on the subject of "Legal Drugs, Illegal Purposes: The Escalating Abuse of Prescription Medications." For a transcript of the hearing see http://www.gpoaccess.gov/chearings/index.html.

[6] A "mention" is the unit of measurement for individual drug reports. For example, an ED visit that involved the use of both hydrocodone and oxycodone would have 2 "drug mentions." In DAWN, up to 4 drugs plus alcohol can be reported for a single ED visit.

[7] Benzodiazepines are prescription drugs used to treat anxiety, insomnia, and seizures.

About DAWN

The **Drug Abuse Warning Network (DAWN)** is a national surveillance system that collects data on drug abuse-related visits to emergency departments (EDs) and drug abuse-related deaths reviewed by medical examiners and coroners. Data on ED visits are collected from a national probability sample of non-Federal, short-stay hospitals, with oversampling in 21 major metropolitan areas. Data from the sample are used to generate estimates for the coterminous U.S. and the 21 metropolitan areas.

ED visits are reportable to DAWN if a patient between the ages of 6 and 97 was treated for a condition associated with intentional drug abuse, including recreational use, dependence, or suicide attempt. Visits involving chronic health conditions resulting from drug abuse are reportable. Abuse of prescription and over-the-counter medications is reportable. Adverse reactions associated with appropriate use of these drugs and accidental ingestion or inhalation of any drug are not reportable.

U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES

U.S. Food and Drug Administration
FDA Talk Paper

FDA Talk Papers are prepared by the Press Office to guide FDA personnel in responding with consistency and accuracy to questions from the public on subjects of current interest. Talk Papers are subject to change as more information becomes available.

T02-38
October 8, 2002

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

SUBUTEX AND SUBOXONE APPROVED TO TREAT OPIATE DEPENDENCE

The Food and Drug Administration (FDA) announced the approval of Subutex (buprenorphine hydrochloride) and Suboxone tablets (buprenorphine hydrochloride and naloxone hydrochloride) for the treatment of opiate dependence. Subutex and Suboxone treat opiate addiction by preventing symptoms of withdrawal from heroin and other opiates.

These products represent two new formulations of buprenorphine. The first of these formulations, Subutex, contains only buprenorphine and is intended for use at the beginning of treatment for drug abuse. The other, Suboxone, contains both buprenorphine and the opiate antagonist naloxone, and is intended to be the formulation used in maintenance treatment of opiate addiction. Naloxone has been added to Suboxone to guard against intravenous abuse of buprenorphine by individuals physically dependent on opiates. Both drugs are supplied in 2 mg and 8 mg tablets which are placed under the tongue and must be allowed to dissolve.

Subutex and Suboxone have been studied in over 2,000 patients and shown to be safe and effective treatments for opiate dependence. Side effects most commonly seen with the use of both drugs include cold or flu-like symptoms, headaches, sweating, sleeping difficulties, nausea, and mood swings. These effects usually peak in the beginning of treatment with Subutex or Suboxone and may last a number a weeks. Clinical data indicate that the risk of serious diminished breathing may be less with buprenorphine than other opioids when used in high doses or in overdose situations. Nonetheless, buprenorphine has been associated with deaths due to diminished breathing, especially when used in combination with alcohol or other Central Nervous System (CNS) depressant drugs, according to reports from France where it has been available for several years.

Based on the potential for abuse of Subutex and Suboxone, FDA and its parent Department of Health and Human Services recommended that the Drug Enforcement Administration (DEA) place the active ingredient, buprenorphine, in Schedule III under the

Controlled Substances Act (CSA). Buprenorphine is considered to have less risk for causing psychological and or physical dependence than the drugs in Schedule II such as morphine, oxycodone, fentanyl, or methadone.

64

Subutex and Suboxone are the first narcotic drugs available for the treatment of opiate dependence that can be prescribed in an office setting under the Drug Addiction Treatment Act (DATA) of 2000. Until recently, opiate dependence treatments in Schedule II, like methadone, could be dispensed in a very limited number of clinics that specialize in addiction treatment. As a consequence, there have not been enough addiction treatment centers to accommodate all patients desiring therapy. Under this new law, medications for the treatment of opiate dependence that are subject to less restrictive controls than those of Schedule II can be prescribed in a doctor's office by specially trained physicians. This change is expected to provide patients greater access to needed treatment.

The sponsor, in collaboration with the FDA and with input from other Health and Human Services agencies, has developed a comprehensive risk management program designed to deter abuse and diversion from its legitimate use in patients and physicians regarding proper use of these drugs, close monitoring of drug distribution channels, and child resistant packaging.

In addition, the provisions of the DATA include limits on the number of patients individual physicians are allowed to treat and special DEA registration for the use of this drug, thus providing additional safeguards as this drug enters the office-based treatment setting.

The risk management program also provides for active and passive surveillance to identify if and when the drugs are being abused. The surveillance will include interviews with substance abusers, monitoring local drug markets, data collection, and the monitoring of adverse event reports. Reports of the results of these surveillance efforts will enable FDA to identify untoward effects from the availability of buprenorphine and, if indicated, to take appropriate actions to protect the public health.

Subutex and Suboxone are manufactured by Reckitt Benckiser Pharmaceuticals.

####

Additional Information on Subutex and Suboxone

Media Contacts | **FDA News Page** | **FDA Home Page**

Office of Public Affairs
Web page created by tg 2002-OCT-08.

FDA Talk Paper

T04-40
September 24, 2004

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

FDA Approves New Extended Release Pain Medication:

Agency Works with Sponsor to Develop an Effective Plan to Reduce Inappropriate Use

The Food and Drug Administration (FDA) announced today the approval of Palladone (hydromorphone hydrochloride) capsules for the management of persistent moderate to severe pain in patients requiring continuous around-the-clock opioid pain relief for an extended period of time.

Palladone is an extended-release formulation that comes in 12, 16, 24, and 32 milligram (mg.) capsules. This drug should only be used in patients who are already receiving opioid therapy and who require a total daily dose of at least 12 mg. of oral hydromorphone or its equivalent. Palladone offers a therapeutic choice for opioid-tolerant patients who might otherwise be candidates for other opioids and who do not achieve satisfactory therapeutic results with these other products.

The active ingredient in Palladone, hydromorphone, is currently a Scheduled II controlled substance, which is the highest level of control for drugs with a recognized medical use. Based on the risks associated with the drug, including the potential for abuse of Palladone, FDA has worked with the sponsor to develop a comprehensive risk management program (RMP).

The RMP was designed with three potential risk situations identified. These are the risks posed by improper dosing, indication, or patient selection; the risk posed by accidental pediatric exposure to the drug; and the risk posed by abuse or diversion of Palladone Capsules.

As a controlled substance in Schedule II of the Controlled Substances Act (CSA), Palladone also comes under the jurisdiction of the Drug Enforcement Administration (DEA), which administers the CSA. Schedule II drugs are subject to manufacturing quotas set by DEA with input on medical need from FDA, distribution tracking, import and export controls, registration of prescribers and dispensers, and written prescriptions without refills.

In addition to the protection afforded patients through the status of Palladone as a controlled substance, the RMP includes provisions for clear and appropriate labeling, and appropriate education of healthcare professionals, patients, and caregivers. In addition, the sponsor has committed to offer appropriate training to sales representatives. To guard against the inappropriate use of the drug, the RMP also establishes a multifaceted program for monitoring and surveillance of abuse. If abuse, misuse, and diversion occur the program includes an array of interventions.

As part of the RMP, a Medication Guide (FDA-approved patient information which is required to be dispensed with each prescription) has been written for patients prescribed Palladone. FDA requires a Medication Guide only when one or more of the following circumstances exists: (1) the drug is one for which patient labeling could help prevent

serious adverse effects; (2) the drug is one that has serious risks of which patients should be made aware because information concerning the risks could affect patients' decision to use, or continue to use the drug; and (3) the drug is important to health and patient adherence to directions for use is crucial to the drug's effectiveness. In addition, the physician labeling for Palladone contains a "black box" warning.

FDA is also part of a larger initiative to reduce diversion and abuse of prescription drugs. On March 1, 2004, the Office of National Drug Control Policy was joined by the Surgeon General, the DEA Administrator, and the FDA Commissioner to announce the *National Drug Control Strategy* . The strategy emphasized new collaborative efforts at the federal, state, and local levels to prevent and reduce diversion and abuse of prescription drugs. This strategy focused on three core tactics: (1) Business Outreach and Consumer Protection, (2) Investigation and Enforcement, and (3) Protecting Safe and Effective Use of Medications. During the approval process for Palladone, FDA incorporated many of the elements of this strategy as exhibited by inclusion of the "black box" warnings on the labeling, the Medication Guide, and the implementation of a RMP.

In addition to the potential for abuse and addiction, respiratory depression is the chief potential risk associated with Palladone, if not properly dosed. Respiratory depression is manifested by a reduced urge to breathe and a decreased rate of respiration, often referred to as "shallow" breathing, and can result in severe effects or fatalities. The risk of respiratory depression is greater in patients not used to taking opiates, and in elderly or debilitated patients.

Palladone must be swallowed whole because chewing, dissolving, or crushing the contents of the capsules leads to the rapid absorption of a potentially fatal dose.

Other common side effects include nausea, vomiting, dry mouth, dizziness, urinary retention, and constipation.

Palladone is manufactured and distributed by Purdue Pharma L.P., located in Stamford, Conn.

####

Generic Neurontin Now Available

MIAMI, Sept. 30 /PRNewswire/ -- For the more than 4 million Neurontin® Capsule prescriptions written in the United States, a low-cost alternative called IVAX Gabapentin Tablets is now available.

IVAX Gabapentin Tablets is the first available FDA-approved generic that contains the same chemical ingredient as Pfizer's Neurontin® Capsules, an epilepsy drug whose U.S. sales reached $2.4 billion in 2003.

IVAX 100 mg, 300 mg and 400 mg Gabapentin Tablets are available through pharmacies nationwide. Neurontin® Capsule prescription holders should ask their health care professionals about switching to IVAX Gabapentin Tablets.

"Neurontin® Capsule prescription holders may save money by switching to IVAX Gabapentin Tablets," said IVAX President and CEO, Dr. Rafick Henein. "The savings are in the form of lower co-payments for the 80 percent or more whose prescriptions could be covered by their health insurance, and even greater savings are possible for those who pay cash because they do not have insurance."

Alfonso Molina, a pharmacist with Walgreens, said, "For more than 20 years, generic pharmaceuticals have been used by millions of people as an effective, affordable alternative to brand-name pharmaceuticals. Generic drugs are strictly regulated by the FDA and deliver the same medication as brand-name pharmaceuticals."

For more information about IVAX Gabapentin Tablets and full prescribing information, visit http://www.gabapentintablets.com or call 1-800-327-4114.

IVAX Gabapentin Tablets are manufactured and distributed by Miami-based IVAX Pharmaceuticals, Inc., which discovers, develops, manufactures and markets both branded and brand-equivalent (generic) pharmaceuticals in the United States and abroad.

Neurontin® is a registered trademark of Pfizer, Inc.

Source: IVAX Pharmaceuticals, Inc.

Oklahoma Medicaid Pharmacy Update

Pharmacy Help Desk Telephone Numbers (405) 271-6349 or 1-800-831-8921
OHCA Website www.ohca.state.ok.us ? Email: Medicaidrx@ohca.state.ok.us

September 28th, 2004

Dear Pharmacy Provider,

Effective October 1st, 2004 Lexxel, Lotrel and Tarka will be available without prior authorization due to supplemental drug rebate agreements with their manufacturers.

Effective October 11th, 2004 SSRIs (Selective Serotonin Reuptake Inhibitors) will be added to step therapy.

Step therapy's goal is to optimize each client's medical therapy with medication that best treats the client's condition given their unique health status and circumstances. Tier 1 medications are preferred as the first step for treating a client's health condition. They are cost effective and are available without prior authorization from OHCA.

Providers who have clients with clinical exceptions may request a prior authorization to skip the step therapy process and receive the Tier 2 drug immediately. Prior authorization forms can be found on the OHCA website at:
http://www.ohca.state.ok.us/provider/billing/forms/pdflib/HCA19_UnivPet03.pdf.

Clients who have been on a Tier 2 drug within 100 days of date of service will be "grandfathered." This allows a client to continue on a Tier 2 drug without a trial on a Tier 1 drug.

Manufacturer's of the drugs listed on Tier 2 did not sign a supplemental drug rebate agreement.

SSRIs (Selective Serotonin Reuptake Inhibitors)	
Tier 1	Tier 2
Fluvoxamine (Luvox)	Citalopram (Celexa)
Paroxetine (Paxil)	Escitalopram (Lexapro)
Paroxetine (Paxil CR)	Fluoxetine (Sarafem)
Paroxetine (Pexeva)	Sertraline (Zoloft)
Fluoxetine (Prozac)	

Effective November 1st, 2004 a prior authorization will be required for brand name drugs that have a state maximum allowable charge.

Thank you for your continued service to Oklahoma's Medicaid clients.