Drug Utilization Review Board

Oklahoma Health Care Authority

4545 N. Lincoln Suite 124

Oklahoma City, Oklahoma 73105

OHCA Board Room

April 12, 2006 @ 6:00 p.m.

THE UNIVERSITY OF OKLAHOMA

THE UNIVERSITY OF OKLAHOMA

MEMORANDUM

TO: Drug Utilization Review Board Members

FROM: Shellie Gorman, Pharm.D.

SUBJECT: **Packet Contents for Board Meeting – April 12, 2006**

DATE: April 6, 2006

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

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

Review of Rheumatoid Arthritis Utilization – **See Appendix C.**

Review of Antiemetic Utilization – **See Appendix D.**

Review of Antibiotic and Related Products Utilization – **See Appendix E.**

Review of Contraceptive Utilization – **See Appendix F.**

New Product Reviews and Notices – **See Appendix G.**

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

Future Business

Adjournment

Drug Utilization Review Board

(DUR Board)

Meeting – April 12, 2006 @ 6:00p.m.

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

AGENDA

Discussion and Action on the Following Items:

Items to be presented by Dr. Whitsett, Chairman:

1. Call To Order

A. Roll Call – Dr. Graham

Items to be presented by Dr. Whitsett, Chairman:

2. Public Comment Forum

A. Acknowledgment of Speakers and Agenda Item

Items to be presented by Dr. Whitsett, Chairman:

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

A. March 8, 2006 DUR Minutes – Vote
B. March 8, 2006 DUR Recommendations Memorandum
C. Provider Correspondence

Items to be presented by Dr. Whitsett, Chairman:

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

A. Retrospective Drug Utilization Review for December 2005
B. Retrospective Drug Utilization Review Response for October 2005
C. Medication Coverage Activity Audit for March 2006
D. Help Desk Activity Audit for March 2006
E. Pharmacotherapy Management Quarterly Report

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

5. Review of Rheumatoid Arthritis Utilization – See Appendix C.

A. Disease and Product Summaries
B. Utilization Review
C. COP Recommendations

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

6. Review of Antiemetic Utilization – See Appendix D.

A. Disease and Product Summaries
B. Utilization Review
C. COP Recommendations

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

7. Review of Antibiotic and Related Products Utilization – See Appendix E.

A. Utilization Review
B. Trends in Antibiotic and Related Products
C. COP Recommendations

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

8. Review of Contraceptive Utilization – See Appendix F.

A. Utilization Review
B. COP Recommendations

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

9. New Product Reviews and Notices – See Appendix G.

A. 30 Day Notice to Prior Authorize Amitiza™
B. Product Summaries

10. FDA and DEA Updates – See Appendix H.

11. Future Business

A. Antimigraine Utilization Review
B. Antiinfectives Utilization Review
C. Antipsychotic Utilization Review
D. Stimulant Follow-Up
E. New Product Reviews and 30 Day Notices
F. OTC Formulary
G. FY05 Summary Utilization

12. Adjournment

APPENDIX A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of MARCH 8, 2006

BOARD MEMBERS:	PRESENT	ABSENT
Brent Bell, D.O., D.Ph.	X	
Dorothy Gourley, D.Ph.	X	
Anetta Harrell, D.Ph.	X	
Kyle Hrdlicka, D.O.		X
Dan McNeill, Ph.D., PA-C	X	
Clif Meece, D.Ph.	X	
James Rhymer, D.Ph	X	
Dick Robinson, D.Ph., Vice-Chair		X
Thomas Whitsett, M.D., Chair	X	

COLLEGE of PHARMACY STAFF:	PRESENT	ABSENT
Leslie Browning, D.Ph./PA Coordinator		X
Metha Chonlahan, D.Ph./Clinical Pharmacist		X
Karen Egesdal, D.Ph./SMAC-ProDUR Coordinator/OHCA Liaison	X	
Kelly Flannigan, Pharm.D../Operations Manager	X	
Shellie Gorman, Pharm.D./DUR Manager	X	
Ronald Graham, D.Ph./Pharmacy Director	X	
Chris Le, Pharm.D., Clinical Pharmacist/Coordinator	X	
Carol Moore, Pharm.D., Clinical Pharmacist		X
Neeraj Patel, Pharm.D., Clinical Pharmacist	X	
Lester A. Reinke, Ph.D.	X	
Visiting Pharmacy Students: (none)		

OKLAHOMA HEALTH CARE AUTHORITY STAFF:	PRESENT	ABSENT
Alex Easton, M.B.A./ Pharmacy Operations Manager	X	
Mike Fogarty, J.D., M.S.W./Chief Executive Officer	X	
Nico Gomez/Director of Governmental & Public Affairs		X
Lynn Mitchell, M.D., M.P.H/Director of Medical Services		X
Nancy Nesser, Pharm.D., J.D./Pharmacy Director	X	
Howard Pallotta, J.D./Director of Legal Services		X
Lynn Rambo-Jones, J.D./Deputy General Counsel III	X	
Rodney Ramsey/Drug Reference Coordinator	X	
Jill Ratterman, D.Ph./Pharmacy Specialist		X

OTHERS PRESENT:

Carol Reyes, Alpharma	Matt Anderson, Alpharma	Jerry Witcher, Forest Labs
Michael Hubert, Pfizer Inc.	Ritchie Sontz, Alpharma	Eve Knisely, Novartis
Lon Lowrey, Novartis	Dale Roof, Takeda	Richard Ponder, Johnson & Johnson
Joanne Hargraves, Schering-Plough	Aaron Walker, Schering-Plough	Angela Asom, M.D., Novo Nordisk
Steve Higgins, TAP Pharmaceuticals	John Rolls, PriCara	Pat Evans, BMS
Toby Thompson, Pfizer	Bob Atkins, Genentech	Mark DeClerk, Lilly
John Burrman, Reckitt Benekiser	Christi Davis O'Brien, Amylin	Joan Colgin, Novo Nordisk
Tony Anata, Novo Nordisk	Mike Cook, Novo Nordisk	

PRESENT FOR PUBLIC COMMENT:

Michael Schwartz, M.D.	Agenda Item No. 5
Marguerite Enlow, Pharm.D.	Agenda Item No. 8

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 Speaker(s) and Agenda Item(s)

Dr. Whitsett acknowledged speaker(s) for Public Comment.

ACTION: NONE REQUIRED.

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

3A: February 8, 2006 DUR Minutes

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

ACTION: MOTION CARRIED.

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

4A: Retrospective Drug Utilization Review Report: November 2005

4B: Medication Coverage Activity Report: February 2006

4C: Help Desk Activity Report: February 2006

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

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 5: **REVIEW OF NARCOTIC ANALGESICS**

For Public Comment, Michael Schwartz, M.D.: *My name is Michael Schwartz. I'm a pain management physician here in Oklahoma City and I was asked to be here to take a look at your review on opioids, and what I would tell you from my perspective as a pain management physician, we approach a little bit different than pain treatment. Whereas with pain treatment we use more short acting opioids than with pain management. We use the extended release long acting, and looking at your information that you have here, I see that you've broken it down on your appendix as to the current quantity limits on particular medications. With many of the patients that we see, we do have higher numbers or units as you look at them, that we use on a monthly basis than what might be seen here with all of the extended release opioids. With the Fentanyl, with morphine, and with items of that nature. So I would appeal to the Board to take a good look at that. From my perspective what we're trying to do is provide the best plasma opioid level 24 hours around the clock and we're able to do that much better with long acting opiods. They are more costly, no doubt about it. Some of those are brand name and they're always going to be more costly that way. Obviously the extended release technology is going to be more expensive as well. As a pain management physician, one of the biggest problems that I have when I have new patients coming to see me is our Lortab problem, hydrocodone. I don't see any limits on that here on a monthly basis. Things that we look at as a pain management physician, obviously we look at safety and quality, efficacious use of a medicine, but we also look at what has street value. The higher the street value, usually the less beneficial it is to me as a physician, and for Oklahoma. And it varies. It depends on which undercover narcotics agent you talk to and how things are going from month to month, but certainly, there's certain ones on that list that have a higher street value and are a bigger problem, and as I see patients come to me, it's not uncommon for me to see a patient that may be taking 40 to 90 Lortab a day. Some of those aren't using that. The problem is with writing at that quantity of Lortab, those can be sold because you can buy those very cheap, obviously. But on the street a 10 mg Lortab can go from anywhere from $40 to $100 a tablet. So there's a big gain on that. Obviously there are generic and that's the appeal because of cost and I understand that, but when we're trying to do pain management and provide the best pain containment we can with the least degree of impairment, and we're always going to do better with the long acting in one or the other classes. So, in looking at your current narcotic quantity limits, I see that you're, and I'm looking at the newer Duragesic, which is brand name only on the 12 mcg, I believe, but then also looking at all of the others in that class. Because we've got several, we've got a couple of extended release morphines and then of course you do have the oxycodone, which oxycontin is what we're talking about, and there is some degree of difficulty in that regard as well, but so I would, my reason for being here is, is to have you, ask you to look very closely at some of those items and the things that we look at and hold valuable in making decisions. Yes sir?*

Dr. McNeill: *I think that if a patient winds up in your practice, diversion is probably not a big issue versus winding up in the emergency room or in a primary care practice, especially with hydrocodone and oxycodone, and certainly I don't think anyone here would want to put limitations on pain management clinics and being able to access and use the medications that you need. Can you envision any way to deal with possibly a diversion, the diversion issue in non-pain management situations? I mean, 25, 26 million dollars a year on this class of drugs, which is huge. Probably one of the highest, isn't it?*

Dr. Nesser: *Yeah, it's in the top ten.*

Dr. McNeill: *I mean, there shouldn't be ... is there a place for quantity limits outside of pain management?*

Dr. Schwartz: *I think perhaps there may be on your short acting immediate release, short acting opioids. Obviously those are the drugs of choice, opioids of choice in urgent care or emergency room, and obviously you're usually going to limit those numbers yourself. Okay. The problem we have of course is that some of those, particularly with hydrocodone, those can be refilled since*

they're a C-III, can be refilled. The problem we talked about this at the Capitol last week on Wednesday, and physicians were saying what can we do to stop this because everybody gets hit on weekends with fake call-ins and it's not uncommon to come in on Monday and find out that you've had 30 scripts filled on Lortab over the weekend, and you weren't even on call. And my only answer to that is, you just don't call, you just don't call medicines in like that. I mean, that's silly to start with. We have to, we can't legislate everything. But so as far as a quantity limit, I mean you know, I guess we could look at other states. Some states have put a limit on that as far as how many you can get per month on the Medicaid programs and programs of that nature. Just simply begin because of the resale. It's, it can be a high, just like Somas and Lortabs, there's just a big, there's a big market out there for those on the street and it's a constant problem. And if, if you're willing to take that chance, a person can make a lot of money if you figure that 30 Lortab at the drugstore will only cost you $19 to $21 and if you can, if you can you know, sell that for three or four thousand dollars, that's a lot of money.

Dr. Meece: *You're talking about the, you said 40 to 90 hydrocodone a day?*

Dr. Schwartz: *Yes sir.*

Dr. Meece: *Okay, does it, is the doctor writing that for them?*

Dr. Schwartz: *Well, it . . .*

Dr. Meece: *See that's where . . .*

Dr. Schwartz: *Yeah. That is a problem and we're trying to address that in pain management, but yeah that does happen, but most of those people are getting, going to more than one doctor, they're going to more than one urgent care, more than one ER, and they can pay that price, so they can get this 30 or get this 40 or whatever it is that they're getting and you know, we had a big grand jury on that just two years ago, and took down a big gang of people who were doing Lortab and soma and then reselling it and buying weapons with it. The Chicago and the L.A. gangs were doing that here in Oklahoma. Oklahoma is number one or number two in the nation on hydrocodone prescriptions.*

Dr. McNeill: *I would imagine . . . there is a difference here between the 25 million, 26 million dollars and well, the 12 million dollars in hydrocodone and oxycodone in putting limits, quantity limits on that, so I couldn't write Ron a script for 320 Lortab, he would be limited to whatever, 40, 80, 120. But what's going to stop, you know, you might get that on, on the Medicaid bill, but then I go to Dr. Bell and get another script, and I'm going to pay for that, but that 13 million dollars, we're paying for that.*

Dr. Schwartz: *Yeah. I mean obviously you could go to more than one physician, but I guess if you set a limit, then there'd only be that one per month that they could be getting, whatever the number you selected that they would be getting through your Medicaid program the way I understand it. Because once they used up their allotted allotment for that month, they wouldn't be able to get any more through your system, but they might pay out of pocket because they certainly could afford to if they're, if they're selling them on the street.*

Dr. McNeill: *But right now there's no limit on the number they can get a month.*

Dr. Schwartz: *True, that is true.*

Dr. Rhymer: *For Medicaid to pay for it, they only allow eight per day, right?*

Dr. Graham: *Days supply.*

Dr. Rhymer: *Eight per day. That's the FDA recommended max, 4000 mg of acetaminophen.*

Dr. Schwartz: *It may be, 4000 is the, is the, considered the highest amount of acetaminophen you want to give per day, but I'm here to tell you that, that I've seen patients taking 150 Lortab a day, 48,000 mg of acetaminophen a day, and their liver functions are perfectly normal. So some people can tolerate a great amount, so using that is not, and some of us can't tolerate very much, so obviously that's a problem.*

Dr. Graham: *I was going to say, we will have a speaker and we'll also have talking about some of these things that, like OBNDD is getting ready to start a new program here in Oklahoma where all schedule drugs are turned into them and that will help on that end because, like he says, we don't know when somebody pays cash for a prescription, all we see is the Medicaid prescriptions. So there's a real problem there with accountability.*

Dr. Schwartz: *There is a problem. Right now, we have it for C-II's but it's lagging and you know that OSTAR program, the computer's still about 80 days behind and so . . .*

Dr. Graham: *But this is even different from OSTAR. It's similar.*

Dr. Schwartz: *Correct.*

Dr. Whitsett: *Do we have a mechanism for recourse should someone feel like they do not have adequate numbers to treat a specific patient? They can petition for that? So I think there is a loophole that if you have a specific patient and you need to go up above that, then you petition the drug utilization review process for and we'll look at that individually and approve it or whatever, you know. And that's, I think that, perhaps the reasonable fail-safe mechanism because as I'm sure you would agree, some physicians are more prone than others to be free with narcotic prescriptions.*

Dr. Schwartz: *That's true. I think one item on here that catches my attention, it doesn't have a page, but it says on "market share". If you look at your market share on there, first, second and third, you can see that 51% says hydrocodone combos, 51%, but yet over, you know, it's 36% in total dollars for oxycodone, so you can look there and you can see where the, the greatest total numbers of percentage are being written, and you can see where the most dollars are being spent as well. And granted, it's a huge number. That's true. It's a lot of money.*

Dr. Whitsett: *Thank you very much. Next, we have a guest speaker, Dr. Hal Vorse, who will talk to us about opiate addiction. He is the Medical Director of the Referral Center, and Dr. Vorse is one of our guests tonight. Thank you.*

Guest Speaker, Hal Vorse, M.D.: *Thank you. My name is Hal Vorse. I practice addiction medicine at the Referral Center. The Referral Center is a 34 bed detox center for alcoholics and drug addicts. I've been Medical Director there for nine years, treating about 12,000 addicts and alcoholics over that period of time. And you can track the incidence of various drugs of addiction. The problem of opiate addiction is increasing dramatically in Oklahoma. Unlike a lot of states, we actually peaked out on the meth epidemic when we went to restricting pseudoephedrine availability two years ago, and we've seen a significant drop in meth addicts and in IV drug users during that time. But we have seen in my facility is about over double the number of opiate addicts that are being admitted for detoxification. I really appreciate the comments of Dr. Schwartz. Of the patients that we're seeing, most of those people are not getting their hydrocodone from physicians. Most of it is on the street or on the internet. Quite a bit, it's pretty easy to get hydrocodone on the internet. And most of the patients we see have not gotten to their addiction*

through the pain management doctors. We have seen some pain management patients to help them who are physically dependent who want to switch over to something else, but it's amazing the severity of pain and the dosage they're taking. They don't exceed the doses that have been prescribed. So the problem's really as mentioned, I think is that people who are in acute care settings are putting folks who are prone to addiction on hydrocodone and then they find out they like it and so they seek it out. Some of them will doctor shop, although I think Oklahoma physicians are becoming more aware of the problem and are probably more sophisticated about it than they were a couple of years ago. One of the problems that I see, and I don't really understand, and that is why the Feds made hydrocodone Class III and oxycodone a Class II. The fact is, in equivalent doses, there is no difference. And in fact, of the opiate addicts that we're seeing today, over two-thirds of them are hydrocodone addicts. And I believe that's just because it's easier to access. It's easier to scam. I think physicians are lulled into the feeling that because the Feds have made it a Class III, it's somehow safer. It is not. I will tell you, someone who's eating 60 Lortabs a day has just a severe addiction as some guy who's shooting up eight bags of heroin a day. And they're just as difficult to detox, and their relapse rate after treatment is just as high, and it's a devastating problem. And among physicians and nurses who become addicted, it's certainly by far the most common drug addiction.

Dr. Bell: *What is data for the relapse rate?*

Dr. Vorse: *That's hard data to come by. It depends on the treatment. With ideal treatment, longterm recovery is pretty high. I'll give you an example. The physicians recovery program of Oklahoma has treated over 600 physicians, dentists, and other healthcare professionals, and we've run at 85% sobriety rate at twenty, at five years post treatment, and that's real, real good. Now does that occur in public sector? No. Part of the reason is that the drug and alcohol treatment in Oklahoma for medically indigent folks is very limited. I turn away as many people as I admit for detox. About 50% of the beds necessary to treat people who have chemical dependency in this state. When I do detox people, of course we have a case management system in which we try to place those patients in longterm treatment, but unfortunately there's a waiting list, sometimes three to four weeks, and if you put those folks back on the street, very few of them actually get the treatment. We just don't have treatment on demand in Oklahoma, so I would say the percentage who get well, particularly with opiate addicts, is probably pretty low. We don't have a system to track these patients in Oklahoma. That's part of our problem. The only data we have is the data that DMHSAS gives us for the number of patients that have detoxed. What percentage of those actually get to the next level of care. But how those folks do at a year or two years, or five years is of course not available in Oklahoma. It's our impression that it's pretty low. There are new advances in the treatment of chemical dependency to confirm pharmacologically that would help improve those statistics, and allow us to more effectively use our treatment dollar in the state. But the fact is, is that we haven't seen an increase in funding for chemical dependency treatment in this state in fifteen years.*

Dr. Whitsett: *How is that funded?*

Dr. Vorse: *Through the Department of Health and Substance Abuse Services, legislative funding. Last . . .*

Dr. Whitsett: *So everyone wouldn't qualify, theoretically?*

Dr. Vorse: *Theoretically, yes. Well, there is for admission to our programs, you have to have 2x poverty or less in order to be qualified for state funded programs. But most chemically dependent folks who are very low bottom have lost the resources in qualifying for that. The people who still have resources, of course, have access to better care and do better. But they also to tend to have a less severe case. There is, there is a problem with severity. Like any other disease, chemical dependency has levels of severity and the sooner you can catch it, diagnose it and treat it, the better patients do. The other thing that you need to know is that the death rate due to prescription drug abuse in Oklahoma has increased 25% in the last year. And a lot of those folks have been receiving methadone. Methadone, methadone has been helpful. It is a harm reduction therapy, substitution therapy; however, methadone is an opiate agonist. It can be overdosed and you can take short acting opiates with it. And a very high percentage of the overdose deaths are associated with methadone use as well. I don't want to overstay my time, so I'll just take questions at this point.*

Dr. McNeill: *Can I ask you about the methadone, since you brought it up? I know the substance abuse department has changed their rules concerning methadone clinics in terms of physician involvement with these patients over the last year. I think the rules went into effect last July, as far as the physician had to do the history and physical, and be more involved in patient care, and the death rate for people on methadone I've know about. But in terms of a treatment modality, if you look at the number of claims for methadone here, it's almost negligible as far as the Medicaid agency goes. Is that a place where there needs to be more improvement through utilization, or is there more . . . if you look at the substance abuse department, it looks like they're trying to place more restrictions on being able to use non-physician providers to help with treatment. Can you comment on that for me?*

Dr. Vorse: *Sure. The DMHSAS system does not have in place, as far as I know, methadone as part of the treatment system and methadone clinics are under them, licensed by them, but they're separate. And as far as, I don't think that a significant number of Medicaid patients actually go through the methadone clinic. I have a prejudice about methadone. I think methadone is for folks who've given up on recovery and when I mean recovery, I mean have gotten totally clean off of addictive drugs. There's three ways to treat this. One is you can detox somebody and give them traditional treatment, or you can put them on a methadone maintenance program and there's no question that it has value to society. There's decreased number of crimes, there's increased occupational activity, there's decreased hospitalizations and utilization of the healthcare system. I question the value to the individual. While, because the methadone patients I've know have not been very happy folks, because they, they, methadone, while it prevents withdrawing, doesn't make people feel good at all. And the problem with opiate addicts and the reason they do so poorly, in my opinion, is their brains have been damaged by the drug, and they don't, they don't produce adequate endorphins because of long opiate use and it takes a long time for that part of their brain to heal to where they can even experience pleasure. And I will tell you that addicts and alcoholics as a group are sensitive folks that don't suffer well, and when life gets tough, they've got to go back to what they know. And so, I feel like that's not the longterm solution. There are other modalities for treatment now, buprenorphine, I think, is going to be the answer pharmacologically, and there's going to be different ways that's utilized of course, and that's relatively new in Oklahoma. There's a few of us that are licensed for it, but . . .*

Dr. Graham: *Dr. Vorse, in your treatment of, you're saying you use some Suboxone, I believe, but what other kind of multiple drugs are you needing required to get someone, you know, off of addition? I mean, there's other drugs I'm sure you have to use a lot with that.*

Dr. Vorse: *Well, it depends on what the drug of addition is. Now what we do at the Referral Center is mostly we do detoxification. With alcoholics, opiate addicts and benzo addicts, we traditionally we've used clonidine, librium and muscle relaxants and other symptomatic treatment. Our dropout rate, it runs overall about 15 to 20%. With opiate addicts, it runs a lot higher. The paradox is that benzo addicts and alcoholics are more apt to die in withdrawal through DT's. Seventeen percent of the folks who go into DT's will die without medical attention, so that's the primary reason they're there to be treated. The opiate addicts rarely every die in withdrawal, but they feel so bad, they don't complete. They tend to go AMA and go back to drug use because they're just so miserable. So one of the things we're trying to do is utilize buprenorphine to improve the detox. The other, the other way it is being used is as a substitute for methadone in longterm maintenance. The third way it's used, the way I prefer to use it is a prolonged detox over a period of several months while they stabilize their recovery. It allows us to alleviate, not only alleviate the symptoms but stabilize their condition, allows us to treat them on an outpatient basis, and much more cost effectively, and allows them to get back to work in a relatively short period of time, like a week. Traditionally, opiate addicts, well even a physician who is addicted to hydrocodone or any other opiate, goes to Atlanta, Georgia for four to six months of inpatient treatment because it's so difficult to get them over those first few months.*

Dr. Bell: *I'm a child and adolescent psychiatrist and I've never had to detox adolescents until the last couple of years and I've had to detox some off Oxycontin. They're getting it from grandma and aunts and uncles . . .*

Dr. Vorse: *Exactly. The Oxycontin story is incredible. The hillbilly heroin that started in rural Maine and it's moved west and it hit here about five years ago. It's the most expensive on the street, matter of fact. And aficionados of the opiate addiction, people who like opiates, love Oxycontin. The problem is, the therapeutic index is so narrow that the overdose death rate is the highest of all drugs out there. And in some states like Pennsylvania, it has the highest death rate of any drug that's being utilized. And again, most of these folks are not getting it from their physician or a physician, they're getting it on the internet or on the street. The patients tell me that they think that a lot of it's coming over the border from Mexico. The other thing I'd like to mention are two drugs that I'm having a real tough time with . . . not controlled. And that's Soma and tramadol, Ultram and Ultracet ER. doctors and other physicians often think that because it's not controlled, it's safe. We've had three physicians in Oklahoma County alone go to longterm inpatient treatment for addiction to tramadol. Tramadol addicts aren't common, but when they get that, well they'll continue to use it in spite of having grand mal seizures. We had a lady come in last month who was taking twenty tramadols a day and Dilantin for her seizures. So the word needs to get out that it is not safe and that people can get addicted. Secondly, soma and somebody mentioned soma. Soma is a real problem because it's not controlled. A lot of physicians don't know that it's metabolized into meprobamate, and that used with opiates and benzos, cause overdose deaths . . . and alcohol of course. And we had a young lady 26 years old I know of that died of an overdose of hydrocodone, soma and alcohol. It's a real problem.*

Dr. Whitsett: *The Bureau of Narcotics going to change tramadol's status?*

Dr. Vorse: *I don't know. The manufacturer notified them in 1998 that it was addictive and they haven't taken any action on it, so I don't . . .*

Dr. Whitsett: *They're studying it?*

Dr. Vorse: *I guess. And you know, the other thing is, is that if I were running this deal, I would have two classes of narcotics. You would either have controlled substances or not. I mean, it's ludicrous to think that a Class III is safer than a Class II. It just, you know. . . . and I think it gives physicians a false sense of security when they prescribe drugs that are other than Class II thinking it's safe and it is not. And I think we ought to eliminate the ability to phone it in or refill it.*

Dr. Whitsett: *Thank you very much Dr. Vorse. We appreciate your being here. We have another person who's with us, Debbie Spaeth, who's with the Oklahoma Health Care Authority, and she's going to, she deals with behavioral health services.*

Guest Speaker, Debbie Spaeth: *Good evening. I'm Debbie Spaeth from the behavioral health department here at the Health Care Authority, and I'm here this evening to talk about our coverage for substance abuse services for those people, or for the members that we cover. Basically, as Medicaid goes, we cover anyone who meets an access one diagnosis for a mental health or substance abuse disorder, and recently there's a SAMHSA grant called Co-Occurring Systems Infrastructure Development Grant that the Department of Mental Health and Substance Abuse Services acquired and Doctors Cline and Minkoff who are over that SAMHSA grant reviewed our policies and felt like they were integrated friendly, meaning basically we cover both mental health and substance abuse services in the outpatient therapy or treatment area. The benefits that we cover are the usual, mental health and substance abuse assessment, treatment plans, therapies, individual group, families, like rehab services, testing, medication trained support, crisis intervention, etc. We also cover inpatient medical detox. Now what we don't cover currently which is needed in the State and we're looking at, well it's one of our Board's top ten priorities is to cover residential treatment for substance abuse. And I think this next year we'll be moving towards a budget proposal for children and adolescents and then moving in the next year towards coverage for adults, and I'm hopeful that those budget approvals will be approved. Of course we have basic criteria for those that qualify for inpatient detox. They have to have the axis I diagnosis for anything but cannabis, nicotine, or caffeine dependence that fits into the chemical dependency realm of the DSM. If the conditions are directly attributable to a substance dependency disorder, determined that the current disabling symptoms cannot be managed or have not been manageable in a lesser intensive treatment program. If the individual requires 24 hour nursing, medical supervision as evidenced by, etc. In the assessment phase, the Health Care Authority doesn't have a particular set of forms that we require providers to complete in the assessment process. We do require the alcohol screening, alcohol severity index to be given as well as for teenagers and children the teen ASI. And that's in collaboration with the Department of Mental Health and Substance Abuse Services guidelines. Between the two agencies we've worked a lot over the past couple of years to make our policies and guidelines consistent so the providers don't have to meet one set for one funding resource and then meet another for another resource. And of course the assessment includes past, present information evaluations, etc. We have certain guidelines between the two agencies for alcohol, drug treatment professionals and of course that includes physicians, psychologists and also those that are licensed to practice alcohol and drug treatment as they're certified for alcohol and drug counseling, and those that are under supervision for their licensure and also do services. They do have to be supervised by a licensed individual. What's to come? I already mentioned that we want to move into residential treatment level services for those needing substance abuse treatment. We also want to look at public entities like the Referral Center that are costing the state 100% state dollars to see if there's a way for Medicaid coverage for that small percentage of the population that would be Medicaid eligible, and also*

moving towards more integration in our policy to cover both mental health and substance abuse services. Any questions regarding substance abuse treatment under Medicaid?
Dr. Whitsett: *Do you feel like we're being able to respond to the demand that's out there and the need? Are we keeping up with it, or staying ahead of the curve?*
Ms. Spaeth: *I think that recently we made a move toward promoting substance abuse treatment for Medicaid members, and between the Department of Mental Health and Substance Abuse Services and our agency, we have seen an increase from, in about the last six months, every month a slow steady increase in the contracted providers for substance abuse services as well as services provided to both children and adults. The majority of our providers are also contracted substance abuse providers with the Department of Mental Health. They have to be accredited through CARF, joint commission COA and have qualified providers.*
Dr. Whitsett: *So we're meeting the need?*
Ms. Spaeth: *I don't we're anywhere meeting the need in this state, but I think it . . .*
Dr. Whitsett: *But it's not our fault?*
Ms. Spaeth: *We've starting getting . . .*
Dr. Whitsett: *. . . a hand on all those that are available to do it . . . means they've got to come to us in the first place. Or do we have a big backlog we can't deal with?*
Ms. Spaeth: *I think we have a lot of rural areas in the state that don't have treatment available. And between the Department and our efforts we're trying to get both youth and family Services agencies, the Department agencies, and with our policy opening up more to integrated treatment, we're hoping we're promoting that people out there will provide this service.*
Dr. Bell: *Do you have a projected . . . you know what my interest is. A projected date for child and adolescent inpatient treatment. I mean, you know, that's so scarce, it's just, it's desperately needed.*
Ms. Spaeth: *Right. We have one residential treatment program in the state and it's 100% state dollars. We'll probably be looking at this year putting in a budget request for July '08. Unfortunately the issue around substance abuse treatment that Dr. Vorse referred to has, it's a longer needed treatment than typical psych based treatment. Psych, you go in, you get stabilized, you come out and hopefully the community services support you maintain, versus chemical dependency it's much longer, and so therefore when you get into budget requests, yeah. Because you want to prevent relapse, so . . .*
Dr. Whitsett: *Thank you very much for informing us.*
Materials included in agenda packet; presented by Dr. Flannigan.
Dr. Meece moved to approve; second by Dr. McNeill
ACTION: MOTION CARRIED.

AGENDA ITEM NO. 6: **VOTE TO PRIOR AUTHORIZE MUSCLE RELAXANT PRODUCTS**
Materials included in agenda packet; presented by Dr. Le.
Dr. Gourley moved to approve with the deletion of criteria no. 1 for tier-2; seconded by Dr. McNeill.
ACTION: MOTION CARRIED.

AGENDA ITEM NO. 7: **VOTE TO PRIOR AUTHORIZE ULTRAM® ER AND ULTRAM® ODT**
Materials included in agenda packet; presented by Dr. Gorman.
Dr. Meece moved to approve; seconded by Dr. Gourley.
ACTION: MOTION CARRIED.

AGENDA ITEM NO. 8: **ANNUAL REVIEW OF PLAVIX®**
For Public Comment, Marguerite Enlow, Pharm.D.: *Yes, thank you Dr. Whitsett, and as he mentioned, I'm Marguerite Enlow, a Pharm.D. in the medical affairs department of Bristol Myers Squibb. I've been here on previous annual reviews of Plavix and reviewed the efficacy and safety of Plavix in patients who've had a recent myocardial infarction, stroke, or peripheral arterial disease, the data head-to-head in the CAPRI trial with aspirin and also in the CURE trial which was an approved indication for acute coronary syndrome in conjuction with aspirin. And tonight I just wanted to say a couple of things. First of all, I wanted to thank the Board and the College of Pharmacy this past year for their efforts in streamlining the prior authorization process for those patients who need it the most, and also I'd just like to offer myself up again if there are any questions or comments that you have about clopidogrel efficacy or safety.*
Dr. McNeill: *I remember last year there was a cardiologist, I think from Baptist, that I think was unfamiliar with 3-day emergency ability to get Plavix after angioplasty on weekends. Have you heard from this fellow or from others? Are they still having problems or has that been figured out?*
Dr. Enlow.: *It's been figured out. Actually, that was Dr. Versad from St. Anthony's and he was concerned about the patients who possibly couldn't get it over the weekend. In addition to educating him about that particular process, the process was streamlined from the Board's perspective as far as the stented patients and not needing an extra level of communication, that they can write it right on the prescription as far as the indication for stent and so forth. It really served to streamline the process and those patients receive their medication in a very timely manner. We've heard from him, but also from other cardiologists, that it is working very well.*
Dr. McNeill: *Could we also put that in the newsletter?*

Dr. Whitsett: *It really has gone well but in the instances where it hasn't then . . . heard about that and people get very angry and rightly so. Because when you are using stents that have a high likelihood of thrombosis early after you place it, then Plavix is really a crucial part of that and they need to go home with it.*
Dr. Enlow.: *Are there any other questions you might have about any recent data or information?*
Dr. Whitsett: *Probably a good thing to do, I'm sure your company's thought about it, is having a going home pack of Plavix that you can send them home with. Because as long as people go home and they're sick on the way or they're tired, they travel 200 miles, and they get there and their pharmacy's closed or, there's all kinds of reasons why people don't always get their meds and to have a going home from the hospital packet with a week's supply of Plavix . . . you're going to be getting it for, you know, keep pushing the envelope longer and longer and I'm sure you know how long people are taking it, and loading them up on the front end with their stents to have something that somebody can hand them, what you take for the week until you get your prescription filled, and something to think about.*
Dr. Enlow.: *Yes, thanks. I'll pass that on up because I have heard about disconnecting a continuum of care whereas the sales force samples in the offices primarily, but the patients who need it immediately are discharged from the hospital and then often that samples are not available at that point of care, and so I think there does need to be some creative thinking about how to get it . . .*
Dr. Whitsett: *. . . in the pharmacy you can write for Plavix sample for one week, Plavix one week samples if someone had product in the package or something that could, I don't know, something to think about.*
Dr. Enlow.: *Okay, thank you.*
Materials included in agenda packet; presented by Dr. Flannigan.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 9 : **ANNUAL REVIEW OF XOLAIR®**
Materials included in agenda packet; presented by Dr. Le.
Dr. Whitsett would like to see how many members in the SoonerCare population might potentially qualify and what their casts are.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 10: **REVIEW OF DIABETES IN THE OKLAHOMA SOONERCARE POPULATION**
Materials included in agenda packet; presented by Dr. Gorman.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 11: **NEW PRODUCT REVIEWS AND NOTICES**
Materials included in agenda packet; presented by Dr. Gorman.
ACTION: NONE REQUIRED.

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

AGENDA ITEM NO. 13: **FUTURE BUSINESS**
13A: Contraceptive Utilization Review
13B: Antiinfectives Utilization Review
13C: Antipsychotic Utilization Review
13D: Annual Reviews
13E: New Product Reviews
13F: OTC Formulary
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: March 24, 2006

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

From: Shellie Gorman, Pharm.D.
Drug Utilization Review Manager
Pharmacy Management Consultants

Subject: DUR Board Recommendations from Meeting of March 08, 2006.

Recommendation 1: Review of Narcotic Analgesics

MOTION CARRIED by unanimous approval.

A quantity limit of 10 units per 30 days to be set on Duragesic®-12 (fentanyl 12.5mcg/hr) to bring it in line with the other fentanyl patch strengths.

Recommendation 2: Vote to Prior Authorize Skeletal Muscle Relaxants

MOTION CARRIED by unanimous approval

Skeletal Muscle Relaxants		
*Tier-1**	*Tier-2*	*Hard PA*
cyclobenzaprine (Flexeril®) baclofen (Lioresal®) tizanidine (Zanaflex®) methocarbamol (Robaxin®) chlorzoxazone (Parafon Forte®, Paraflex®) orphenadrine (Norflex®)	metaxolone (Skelaxin®)	carisoprodol (Soma®) carisoprodol w aspirin carisoprodol, ASA, codeine

*Brand products are subject to the Brand Name Override where generic is available.

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

1. ~~FDA approved indication. Skeletal muscle relaxants are recommended as adjunct to rest, and/or physical therapy for the relief of musculoskeletal pain.~~
2. Documentation of failed withdrawal attempt within past three months defined as increase in pain and debilitating symptoms when medication was discontinued.
3. Failure with at least two Tier-1 medications within the past 90 days defined as no beneficial response after at least two weeks of use during which time the drug has been titrated to the recommended dose.
4. Approvals will be for the duration of three months, except for members with chronic diseases such as multiple sclerosis, cerebral palsy, muscular dystrophy, paralysis, or other chronic musculoskeletal diagnosis confirmed with diagnostic results, in which case authorizations will be for the duration of one year.

The following criteria are recommended for approval of carisoprodol or carisoprodol combination products:

A cumulative 90 therapy day window per 365 days will be in place for these products, further approval will be based on the following:

1. An additional approval for 1 month will be granted to allow titration or change to a Tier1 muscle relaxant, further authorization will not be granted, or
2. Indication of multiple sclerosis, cerebral palsy, muscular dystrophy, and/or paralysis with approvals granted for the duration of one year.

Recommendation 3: Vote to Prior Authorize Ultram ER and ODT

MOTION CARRIED by unanimous approval.

The College of Pharmacy recommends Prior Authorization of Ultram® ER and ODT.

Criteria for approval of the ER formulation would include

1. an FDA approved diagnosis for the use of Ultram® ER,
2. a diagnosis indicating that the member has a condition that requires extended pain treatment with an around-the-clock dosing schedule,
3. the reason immediate release tramadol is inappropriate, and
4. the physician's signature.
5. Maximum covered dose of 300 mg daily due to lack of efficacy and increased risk for side effects and seizures.

Criteria for approval of the ODT formulation would include

1. an FDA approved diagnosis for the use of Ultram® ODT,
2. a diagnosis indicating that the member has a condition that prevents them from swallowing tablets,
3. and the physician's signature.

Approvals will be for 90 days, with the exception of members with a cancer related diagnosis where an approval will be granted for one year.

The College of Pharmacy also recommends quantity limits of

1. 30 units for 30 days for the ER, and
2. 240 units for 30 days for the ODT (unless another FDA dosage is approved).

Recommendation 4: Annual Review of Plavix

No action required.

Recommendation 5: Annual Review of Xolair

No action required.

SWEETEN MEDICAL CLINIC
3400 TUXEDO BLVD., SUITE G
BARTLESVILLE, OK 74006
PHONE: (918)333-3136

MARCH 7, 2006

TO WHOM IT MAY CONCERN:

I HAVE HAD A GOOD DEAL EXPERIENCE WITH ULTRAM FOR PAIN CONTROL, & I FEEL THE NEWLY RELEASED "ER" PREPARATION IS A DEVISED IMPROVEMENT OF AN ALREADY EXCELLENT MEDICATION.

IT IS EFFECTIVE, WITH LOW ABUSE POTENTIAL. I STRONGLY PREFER THAT, IT NOT BE A PRIOR AUTH DRUG.

THANK YOU,

ROBERT SWEETEN M.D.

2039 W. Edison St.
Tulsa, OK 74127-5254
Telephone: (918) 584-6326
Facsimile: (918) 585-9627

GILCREASE MEDICAL CENTER, PC

Gary R. Lee, M.D.
Board Certified
Independent Medical Examiner
Sports Medicine

March 6, 2006

To Whom It May Concern:

I have had experience with Ultram as an excellent pain medication with low abuse potential and adequate pain control for mild to moderate acute pain related to injuries. I prefer this medication over Hydrocodone and Oxycodone for acute pain. Now that Ultram Extended Release is available, I would request that this be provided on Medicaid without prior authorization, as this medication would allow for me to treat chronic pain with a much greater safety profile and lower abuse potential than extended release medications such as Oxycontin, Methadone and Morphine. Thank you for your consideration in this matter.

Sincerely,

Gary R. Lee, M.D.
GRL/mew

APPENDIX B

Retrospective Drug Utilization Review Report

Claims Reviewed for December 2005

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Total # of messages returned by system when no limits were applied	117,298.	115,793	1,091,679	53,095
Limits which were applied	Established, Major, Females, Age 53-65	Narcotics, Females, age 31-33 years	Contraindicated, Age 51-65 years, Asthma	High dose, Centrally acting SMR, Males and Females, Age 22-40
Total # of messages after limits were applied	47	258	14	62
Total # of members reviewed after limits were applied	76	171	13	15

LETTERS			
Prescribers		**Pharmacies**	
Sent	**Responded**	**Sent**	**Responded**
181		150	

Retrospective Drug Utilization Review Report

Claims Reviewed for October 2005

Module	Drug Interaction	Duplication of Therapy	Drug-Disease Precautions	Dosing & Duration
Limits which were applied	Established, Major, Males 50-65	Acetamenophen, Females, Age 22-26, abuse and no abuse potential	Contraindicated, age 22-35, with Asthma	High dose, Digitalis, Males and Females, Age 0-65

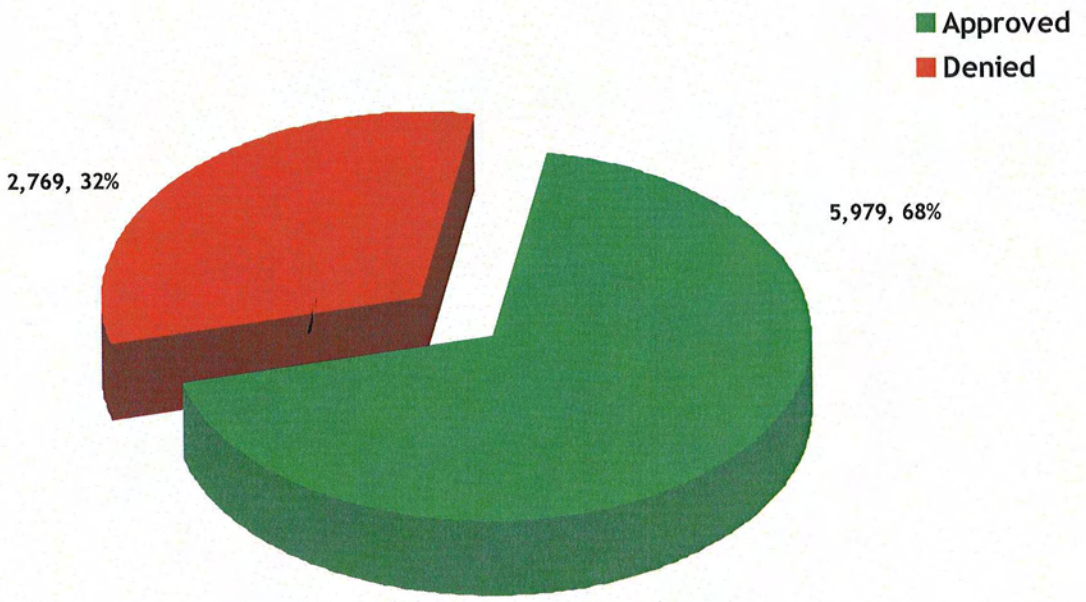
Response Summary (Physician)
Letters Sent: 185
Response Forms Returned: 108
The response forms returned yielded the following results:

19 (18%)	*Record Error—Not my patient.*
21 (19%)	*No longer my patient.*
8 (7%)	*Medication has been changed prior to date of review letter.*
26 (24%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
15 (14%)	*I am aware of this situation and will plan to continue monitoring therapy.*
19 (18%)	*Other*

Response Summary (Pharmacy)
Letters Sent: 134
Response Forms Returned: 105
The response forms returned yielded the following results:

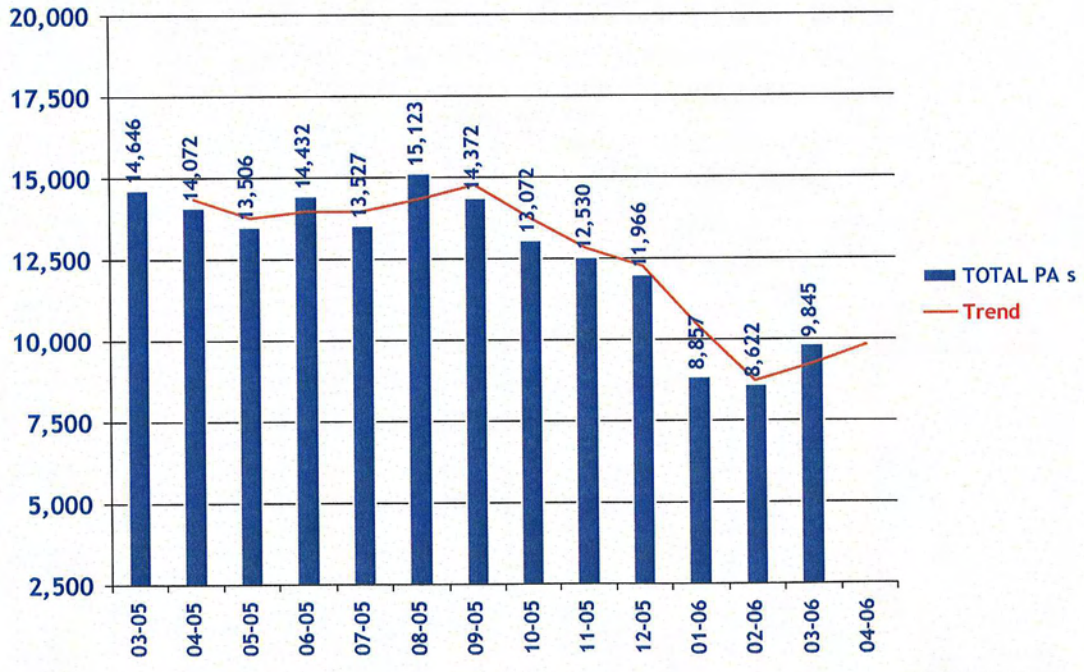
2 (2%)	*Record Error—Not my patient.*
6 (6%)	*No longer my patient.*
10 (10%)	*Medication has been changed prior to date of review letter.*
33 (31%)	*I was unaware of this situation & will consider making appropriate changes in therapy.*
37 (35%)	*I am aware of this situation and will plan to continue monitoring therapy.*
17 (16%)	*Other*

PRIOR AUTHORIZATION ACTIVITY REPORT
March 2006



PHARMACY Management Consultants

PRIOR AUTHORIZATION REPORT
March 2005 - March 2006



PHARMACY Management Consultants

Date Processed: Monday, April 03, 2006

Activity Audit for

March 01 2006 Through March 31 2006

Date	Antiulcers app.	Antiulcers den.	Anxiolytic/ Hypnotics app.	Anxiolytic/ Hypnotics den.	Antihistamine app.	Antihistamine den.	Growth Hormones app.	Growth Hormones den.	Stimulant app.	Stimulant den.	Nsaids app.	Nsaids den.	ACE Inhibitors app.	ACE Inhibitors den.	HTN Combos app.	HTN Combos den.	Calcium Channel Blockers app.	Calcium Channel Blockers den.	Plavix app.	Plavix den.	ARB app.	ARB den.	Anti-depressants app.	Anti-depressants den.	Daily Total
App.	9		2781		1087		36		821		36		11		1		34		168		2		141		
Den.		7		483		781		3		273		119		25		4		75		23		0		196	
Average Length of Approvals in Days	12		94		97		162		199		294		167		363		284		348		365		208		

Changes to existing PA's	719
Total (Previous Year)	14646

*** Denial Codes**

762 = Lack of clinical information	25.42%
763 = Medication not eligible	1.23%
764 = Existing PA	1.66%
772 = Not qualified for requested Tier	3.39%
773 = Requested override not approved	13.80%

SUPER PA's

Admitted to Nursing Home	28
Early Refill Attempts	27017
Dosing Change	373
High Dose	12
Lost/Broken Rx	106
Stolen	9
Other	50
Wrong D.S. on Previous Rx	13
Quantity vs. Days Supply	937
Brand	105
-- Approved	44
-- Denied	43

Monthly Totals

	Number	Percent of Total
Approved	5972	60.66%
Additional PA's	4	0.04%
Emergency PA's	3	0.03%
Duplicates	32	0.33%
Incompletes	1065	10.82%
Denied *	2769	28.13%
Total	9845	100.00%

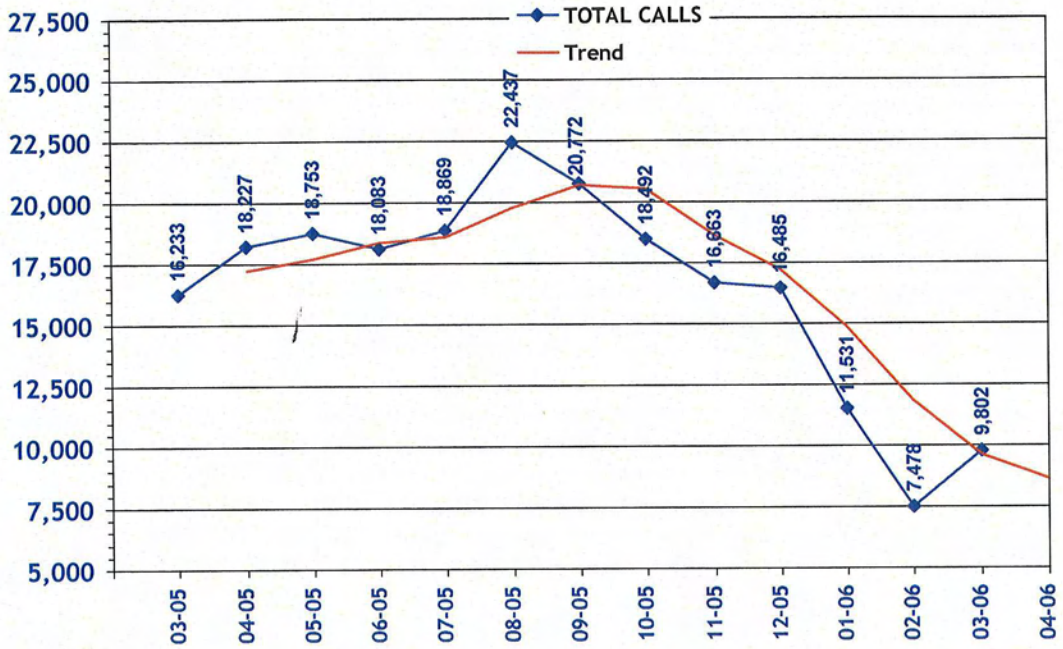
Daily Average of 447.50 for 22 Days

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

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

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

CALL VOLUME MONTHLY REPORT
March 2005 - March 2006



PHARMACY Management Consultants

Pharmacotherapy Management Program
Quarterly Report FY'06
July 2005 – March 2006
Oklahoma Health Care Authority

	MEMBER PROFILES REVIEWED		PRIOR AUTHORIZATIONS				COMMUNICATIONS	
Month	New Members	Established Members	Total	Approved	Denied	Incomplete	Letters	Calls
July 2005	94	47	818	540	44	234	357	29
Aug 2005	103	73	830	585	38	257	482	45
Sept 2005	73	32	962	643	45	274	230	37
Oct 2005	25	28	805	561	53	191	152	37
Nov 2005	28	66	848	634	29	185	236	47
Dec 2005	31	52	861	648	39	550	156	29
Jan 2006	23	76	299	190	22	87	229	22
Feb 2006	17	47	158	94	5	59	136	28
March 2006	29	51	271	177	32	62	174	38
April 2006								
May 2006								
June 2006								
Totals								
1st Quarter	270	152	2,660	1,768	127	765	1,069	111
2nd Quarter	84	146	2,514	1,843	121	550	554	113
3rd Quarter	69	174	728	461	59	208	539	88
4th Quarter								
Totals	423	472	5,902	4,072	307	1,52	2,152	312

APPENDIX C

Rheumatoid Arthritis
Oklahoma Medicaid
April 2006

Introduction
Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by uncontrolled proliferation of synovial tissue and a wide array of multisystem comorbidities.[1] Factors that are involved in RA include 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.
It is estimated that RA affects about 0.8% of the population worldwide. Women are twice as likely to develop the disease more than men. RA is responsible for an estimated 250,000 hospitalizations and 9 million physician visits each year.[2]
Progression of RA is monitored according to the American College of Rheumatology (ACR) criteria based on changes in specific symptoms and laboratory findings.

Lab Abnormalities[3]

Laboratory test	Associated findings
C-reactive protein*	Typically increased to 0.7picograms/ml; may be used to monitor disease course
Erythrocyte sedimentation rate*	Often increased to >30mm per hour; may be used to monitor disease course
Hemoglobin/hematocrit*	Slightly decreased; normochromic anemia; also may be normocytic or microcytic
Liver function*	Normal or slightly elevated alkaline phosphate
Platelets*	Usually increased
Radiographic findings of joints*	May be normal or show osteopenia or erosions near joint spaces in early disease
Rheumatoid factor*	Negative in 30% of patients in early illness; not an accurate measure of disease progression
White blood cell count*	May be increased
Anticyclic citrullinated peptide antibody	Correlates well with disease progression; increases sensitivity when used in combination with rheumatoid factor; not readily available in many laboratories
Antinuclear antibody	Limited value as a screening study for RA
Complement levels	Normal or elevated
Immunoglobulins	Elevated alpha-1 and alpha-2 globulins possible
Joint fluid elevation	Consider if an affected joint can be tapped and diagnosis is uncertain
Urinalysis	Microscopic hematouria or proteinuria may be present in many connective tissue

*** Recommended for initial evaluation for rheumatoid arthritis**

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 ACR, the diagnosis of RA requires confirmation of at least four of the following criteria[4]:

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

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 <50 ml/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	25-50 mg 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
Most Recent DMARDs				
Rituximab (Rituxan)		375mg/m^2 IV infusion once weekly for 4 or 8 doses	Fatal Infusion reaction, tumor lysis syndrome, severe mucocutaneous reaction, Hepatitis B reactivation, infections, bowel obstruction and perforation, cardiac arrythmias	s/sx of infection, SCr
Abatacept (Orencia)		<60kg=500 mg; 60-100kg=750 mg; >100kg=1gram 30 minute infusion given at 2 and 4 weeks after 1st infusion; then every 4 weeks	Hypersensitivity, HA, upper respiratory tract infection, sore throat, nausea	s/sx of infection

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[5]

Trend in DMARDs Utilization

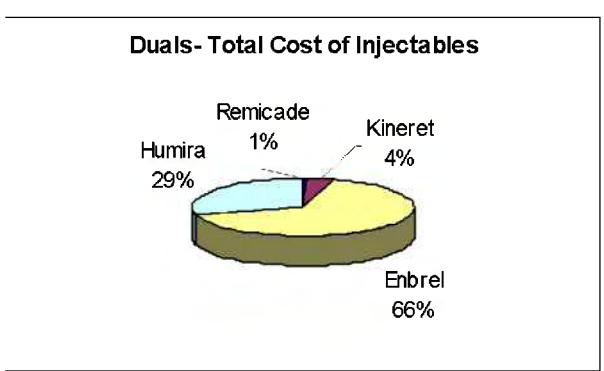
	Calendar Year 2004	Calendar Year 2005	Percent Change
Total Claims	**9,625**	**11,461**	**19%**
Plaquenil	2,914	3,323	14%
Azulfidine	1,361	1,467	8%
Rheumatrex	10	4	-60%
Ridaura	47	29	-38%
Gold salt	4	5	25%
Imuran	1,203	1,454	21%
Neoral	843	730	-13%
Cuprimine	59	36	-39%
Arava	728	1,253	72%
Enbrel	1,605	2,154	34%
Remicade	23	18	-22%
Remicade OP	95	148	56%
Kineret	162	134	-17%
Humira	571	706	24%

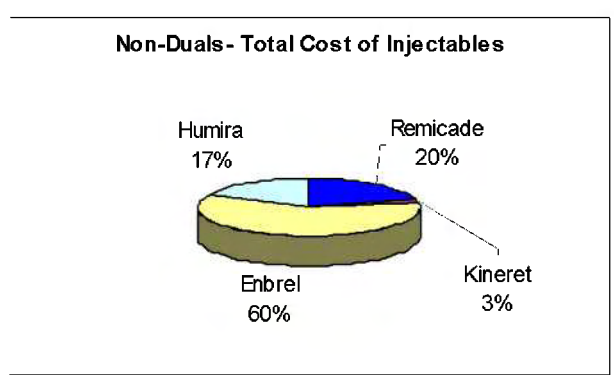
	Calendar Year 2004	Calendar Year 2005	Percent Change
Total Cost	**$ 4,187,260.00**	**$ 5,457,100.71**	**30%**
Plaquenil	59,348.97	55,242.90	-7%
Azulfidine	32,155.05	31,013.16	-4%
Rheumatrex	380.20	131.21	-65%
Ridaura	9,146.69	6,325.70	-31%
Gold salt	542.24	745.43	38%
Imuran	45,919.13	34,961.60	-24%
Neoral	261,153.60	232,439.73	-11%
Cuprimine	6,959.51	5,593.82	-20%
Arava	318,124.97	457,277.99	44%
Enbrel	2,007,046.67	2,923,329.64	46%
Remicade	77,570.85	31,683.30	-59%
Remicade OP	245,271.88	401,440.32	64%
Kineret	200,752.06	158,571.07	-21%
Humira	922,888.18	1,118,344.84	21%

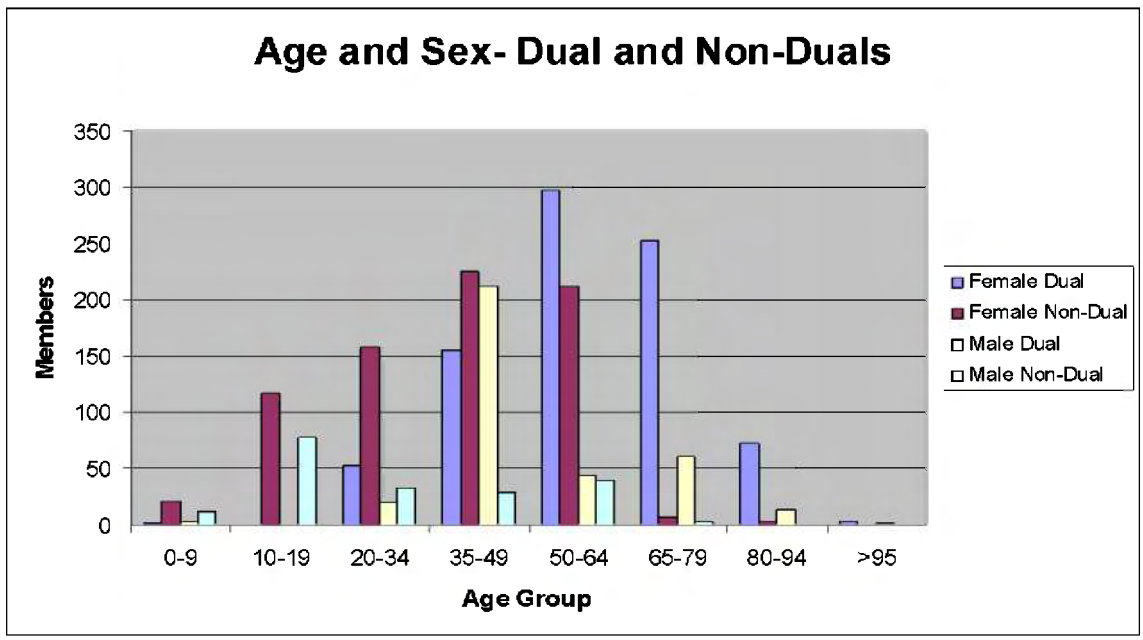
	Calendar Year 2004	Calendar Year 2005	Percent Change
Cost Per Claim	**435.04**	**467.15**	**7%**
Plaquenil	20.36	16.62	-18%
Azulfidine	23.62	21.14	-10%
Rheumatrex	38.02	32.80	-14%
Ridaura	194.61	218.13	12%
Gold salt	135.56	149.09	10%
Imuran	38.17	24.05	-37%
Neoral	309.79	318.41	3%
Cuprimine	117.96	155.38	32%
Arava	436.98	364.95	-16%
Enbrel	1,250.50	1,357.16	9%
Remicade	3,372.65	1,760.17	-48%
Remicade OP	2,581.81	2,712.43	5%
Kineret	1,239.21	1,183.37	-5%
Humira	1,616.27	1,584.06	-2%

Duals vs. Non-Duals

	Duals	Non-Duals
Number of Members	1010	936
Total Cost	$ 2,975,028.80	$ 2,482071.91
Total Claims	6,411	4,902







Management of Rheumatoid Arthritis (Guidelines based on ACR 2002 update)[6]

- 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 and Upcoming Therapies for Rheumatoid Arthritis

Table 1
New therapies for rheumatoid arthritis

Therapeutic agent	Trade name	Mechanism of action	Stage in development[a]
Cytokine targets			
Infliximab	Remicade	TNF-α inhibitor	FDA-approved
Etanercept	Enbrel	TNF-α inhibitor	FDA-approved
Adalimumab	Humira	TNF-α inhibitor	FDA-approved
Anakinra	Kineret	IL-1 receptor antagonist	FDA-approved
IL-1 TRAP	—	IL-1 inhibitor	Phase-2 trials
Tocilizumab	Actemra	IL-6 receptor inhibitor	Phase-3 trials
IL-15 monoclonal antibody (HuMax IL15/AMG 714)	—	IL-15 inhibitor	Phase-2 trials
IL-12 monoclonal antibody	—	IL12 p40 subunit inhibitor	Preclinical
IL-18 binding protein	—	Il-18 antagonist	Phase-2 trials
Anti-MCP1 monoclonal antibody (ABM912)	—	MCP-1 inhibitor	Phase-2 trials with negative results
CCR1 antagonist	—	CCL3/CCL5 chemokine blocker	Phase-2 trials
B-cell targeting			
Rituximab	Rituxan	$CD20^{+}$ B-cell depleting agent	Awaiting FDA approval
Belimumab	Lymphostat B	BLyS inhibitor	Phase-2 trials
T-cell targeting			
Abatacept	Orencia	Inhibitor of T-cell activation	FDA-approved
Osteoclast inhibitors			
Zolindronic acid	Zometa	Inhibitor of farnesyl pyrophosphate synthase	Phase-2 trials
RANKL monoclonal antibody (AMG 162)	—	Inhibitor of RANKL-induced osteoclast activity	Preclinical
Small molecules			
p38 MAP kinase inhibitor (VX-702 and BIRB796)	—	Inhibits expression of proinflammatory cytokines	Phase-2 and -3 trials
HMGCoA reductase inhibitors	—	Inhibits Th1 responses	Phase-2 trials

Abbreviation: Th1, T helper–1 cells.
[a] As of October 2005.

Reference: New Therapeutics in Rheumatoid Arthritis. Rindfleisch J.D, Muller, D.M[7]

Rituxan® was approved by the FDA on February, 28, 2006 to be used in combination with Methotrexate for the treatment of moderate to severe rheumatoid arthritis.

Orencia® was approved by the FDA on December, 26, 2005 for the treatment of moderate to severe rheumatoid arthritis. Orencia® may be used as monotherapy or concomitantly with DMARDs other than TNF antagonists. Orencia® should not be administered concomitantly with TNF antagonists and is not recommended for use concomitantly with anakinra.

Current Literature

Current standard of care is Methotrexate alone, followed by the addition of a DMARD. Based on trials such as the Aspire, TEMPO, PREMIER, there is evidence that supports the use of Methotrexate in combination with a DMARD such as Remicade, Enbrel, Kineret and Humira. (See table next page)

Remicade is approved as a first line agent with Methotrexate for moderate to severe rheumatoid arthritis.

Recommendation

With Remicade being approved as a first line agent with Methotrexate and the increased evidence supporting the use of combination therapy, the College of Pharmacy recommends to continue monitoring this drug category.

Table 1
Efficacy of methotrexate, tumor necrosis factor–inhibitors and the combination tumor necrosis factor–inhibitor and methotrexate in early rheumatoid arthritis

Trial				Population		Clinical outcome (% of patients)				
Name [Ref.]	Type	Comparison	Follow-up (wk)	No. of patients	Disease duration	Regimen	ACR50	ACR70	Remission (DAS_{28} < 2.6)	Radiologic outcome ΔSHS[a] (mean)
Aspire [23]	RCT	MTX alone vs. MTX + infliximab	54	1049	≥ 3 mo and ≤ 3 y	MTX + placebo	32	21	15	3.7
						MTX + IFX 3 mg/kg	46*	33**	21***	0.4*
						MTX + IFX 6 mg/kg	50*	37*	31*	0.5*
TEMPO [30]	Subanalysis of RCT	MTX + etanercept vs. either drug alone	104	229 (of 682)	≥ 6 mo and ≤ 3 y	MTX + placebo	43	23	19	—
						Etanercept + placebo	58	33	34	—
						MTX + etanercept	69****	44****	43	—
PREMIER [39]	RCT	MTX + adalimumab vs. either drug alone	104	799	< 3 y	MTX	43	28	25	10.4
						Adalimumab	37	27	25	5.5******
						MTX + adalimumab	59*****	47*****	50*****	1.9*****

Abbreviations: MTX, methotrexate; RCT, randomized controlled trial.

[a] Progression of joint damage as measured with Sharp-Van der Heijde score.

* $P < 0.001$ compared to MTX + placebo; ** $P = 0.002$ compared to MTX + placebo; *** $P = 0.065$ compared to MTX + placebo; **** $P < 0.05$ compared to MTX alone; ***** $P < 0.001$ compared to MTX alone and to adalimumab alone; ****** $P < 0.001$ compared to MTX alone.

References:

[1,2,3] Rindfleisch JA, Muller D; Diagnosis and Management of Rheumatoid Arthritis. American Family Physician. 72 (6): 1037-1047, 2006 September
[4,6] American College of Rheumatology. Arthritis and Rheumatism. 46(2): 328-346, 2002 February
[5] Shargel: Comprehensive Pharmacy Review., 5th ed. Copyright © 2004 Lippincott Williams and Wilkins
[7] Savage C, St. Clair E; New Therapeutics in Rheumatoid Arthritis. Rheumatic Disease Clinics of North America. 32: 57-74, 2006
[8] Vries-Bouwstra J, Dijkmans B, Brredveld F; Biologics in Early Rheumatoid Arthritis. Rheumatic Disease Clinics of North America. 31: 745-762, 2005

APPENDIX D

Drug Utilization Review – Antiemetics

Oklahoma Health Care Authority
April 2006

Introduction

Nausea and vomiting are common symptoms which may be attributed to a wide range of clinical conditions and illnesses. Symptoms may result from infection, food poisoning, motion sickness, gastrointestinal obstruction, head injury, medication, pregnancy, or migraines.

More severe presentations of nausea and vomiting may be associated with recent cardiovascular events, hepatic or renal impairment, central nervous system disorders, or some forms of cancer. Mild symptoms are discomforting but usually are short in duration and readily treatable with simple but inexpensive non-pharmacologic or pharmacologic therapy. Severe nausea and emesis may cause dehydration, malnutrition, metabolic disorders, or premature death particularly in high risk infants and children. Clinical diagnosis and management poses more of a challenge depending on the etiology, severity, duration and frequency of the episode. Chronic nausea and vomiting is defined as symptoms lasting over 1 month.[13] In addition to physiological risk factors, psychological risk factors can be associated with chronic unexplained nausea and vomiting. Successful cost-effective management can have a substantial effect on therapeutic outcomes, overall health care costs, and patient quality of life. Prevention is the preferred approach to alleviate symptoms rather than treatment after nausea and vomiting has been established.

Definitions[1, 2]

- **Nausea** – is the subjective unpleasant sensation in the throat or epigastric region associated with flushing, tachycardia, and awareness of the urge to vomit.
- **Emesis** (Vomiting) – is characteristic of contraction of the abdominal muscles, descent of the diaphragm, and voluntary or involuntary forceful expulsion of gastric contents through the mouth.
- **Retching** – involves the spasmodic contractions of the diaphragm, thoracic, and abdominal wall muscles without expulsion of gastric contents.

Classification and Epidemiology[2, 3]

- **Nausea and Vomiting during Pregnancy (NVP)**
  - 65 to 80% of the women in the United States.
  - Approximately 4 million affected annually.
  - Usually begins in the 1st Trimester lasting about one month.
  - 50% have relief by 14th week of gestation; 90% by 22nd week
  - Incidence decreases with age.
  - Less than 1% experience ***hyperemesis gravidarum*** which is characteristic of severe uncontrollable vomiting leading to acute starvation, dehydration, metabolic disturbances, and possible loss of pre-pregnancy weight.

- **Post-Operative Nausea and Vomiting (PONV)[1, 3]**
  - Over 60% of the 79 million surgical procedures are performed in ambulatory care setting annually leading to 20 to 30% incidence rate.
  - Approximately $1.2 billion a year in PONV costs in the United States.
  - Risk factors include: Female gender, history of motion sickness or PONV, non-smoker, use of opioid medications, type and duration of anesthesia, and type of surgery.
  - 35 to 50% incidence in school-aged pediatric patients

- **Chemotherapy-Induced Nausea and Vomiting (CINV)[1]**
  - Chemotherapeutic agents frequently cause nausea and vomiting but vary according to type of cytotoxic agent, dose, schedule of therapy, and presence of psychological factors.
  - Types of CINV:
    - ***Acute*** – episodes within the first 24 hours after chemotherapy.
    - ***Delayed*** – episodes after the first 24 hours; may last up to 120 days.
    - ***Refractory*** – episodes despite prophylactic or acute therapy requiring rescue therapy.
    - ***Anticipatory*** – episodes resulting from a learned behavioral component following previous therapy.
  - Therapy selection should be based on entire treatment cycle rather than separate episodic treatment phases during chemotherapy.

- **Radiation-Induced Nausea and Vomiting (RINV)[1]**
  - RINV is generally not as common as CINV. The exact mechanisms of nausea and vomiting caused by RINV are not fully understood or well studied.
  - In general, the majority of patients undergoing radiation therapy will not require pharmacologic treatment for nausea and vomiting. Episodes become less predictable and severe in contrast to CINV.
  - Risk factors include:
    - ***Site of irradiation***
    - ***Dose of radiation***
    - ***Rate of radiation exposure***
    - ***Field size of target area***
  - Radiation therapy may accompany treatment cycle of chemotherapy which may lead to increase incidence and severity of nausea and vomiting.

- **Refractory, Anticipatory, and Breakthrough**
  - ***Refractory*** nausea and emesis occurs despite optimal prophylactic or acute treatment in previous treatment cycles.
  - Psychogenic factors may result in ***anticipatory*** nausea and vomiting due to learned behavioral event or previous treatment experience.
  - ***Breakthrough*** nausea and vomiting occurs following inadequate or ineffective preventative treatment.

FDA Indications[4] and Treatment

Prevention is always the preferred treatment over therapy of established nausea and vomiting. Various non-pharmacologic and pharmacologic treatment modalities exist to alleviate symptoms of nausea and vomiting and improve quality of life.

Several guidelines have been developed for management of CINV, RINV, PONV, and management of nausea and vomiting in pregnancy. Evidence has shown that adherence to guidelines can result in quality cost-effective health care.[5] It is estimated that 52% of physician's believe that the use of guidelines would improve the quality of patients' care.[5] The inadequate or excessive use of antiemetics may lead to refractory episodes and unnecessary medical expenses due to wasted drug or rescue therapy. Approximately 30 to 50% of patients do not receive appropriate antiemetic treatment.[5]

- Non-pharmacologic
  - Drink clear or ice-cold drinks; gradually increasing amounts
  - Eat light and bland foods
  - Avoid high-fat or spicy meals and sweets
  - Eat smaller more frequent meals
  - Avoid strenuous activity
  - Avoid brushing teeth after eating
  - Do not mix hot and cold foods
  - Accupressure or Transcutaneous Electrical Nerve Stimulation (TENS) Device
  - Ginger
  - Avoidance of sensory stimuli (i.e. odors, light, pain)
  - Investigational strategies (i.e. music therapy, hypnosis, muscle relaxation, diversion therapy, guided imagery and biofeedback)
- Pharmacologic **(OTC)**
  - Vitamin B_6 (pyridoxine) FDA-approved for nausea and vomiting prophylaxis in pregnancy in combination with doxylamine (Unisom) in August 1999.
  - Bismuth subsalicylate (Kaopectate, Pepto-Bismol) used for upset stomach, anti-diarrheal, nausea and vomiting.
  - Dimenhydrinate (Dramamine) and meclizine (Dramamine Less Drowsy) for use in motion sickness.
- Pharmacologic **(RX)**

Medication			**PONV***		
Ondansetron	Y	Y	Y	N	Prophylaxis only in CINV
Granisetron	Y	Y	Y	N	Prophylaxis only except in PONV
Dolasetron	Y	Y	Y	N	Prophylaxis only except in PONV (injection form only)
Palonosetron	Y	N	N	N	Prophylaxis only in CINV
Emend	Y	N	N	N	Adjunct prophylaxis only in CINV with steroid and 5HT3
Marinol	Y	N	N	N	Refractory treatment; 3rd Line

- Pharmacologic **(CINV)**
  - Treatment of CINV is based on the emetic potential of chemotherapeutic agent.
  - First-line approach utilizes 5HT3 antagonist as prophylactic treatment and adequate use of corticosteroid or substance P antagonist. [10]

Chemotherapy Induced Nausea and Vomiting (CINV) Emetic Risk Category[6]			
Emetic Potential	Acute Phase (Day 1)	Followed by ➔	Delayed Phase (Day 2 or more)
High	5HT3 + Dex	➔	Dex + MCP or 5HT3
Moderate	5HT3 + Dex	➔	Dex + 5HT3 or MCP or monotherapy of each
Low	Monotherapy**	➔	None
Minimal	None	➔	None
**dexamethasone, dopamine antagonists, phenothiazines, butyrophenones (*5HT3* serotonin receptor antagonist, *MCP* metoclopramide, *Dex* Dexamethasone)			

Chemotherapy Induced Nausea and Vomiting (CINV) Drug Regimens[6]			
Drug (s)	**Acute Phase** I.V. (mg/kg)/mg	Oral (mg)	**Delayed Phase** Oral (mg)
Dolasetron	1.8/100	100	100 daily
Granisetron	0.01/1	2	1 twice daily
Ondansetron	0.15/8	24-32	8 twice daily
Tropisetron	5	5	5
Dexamethasone			
High risk	20	20	8 twice daily (days 2-4)
Moderate	10-20	12-20	4-8 twice daily (days 2-3)
Low risk	4-20	4-20	None
Metoclopramide	None	None	20-40 twice to four times daily

  - Nausea and vomiting may recur at various times throughout the treatment cycle which may require rescue therapy from the same or alternative pharmacologic class.
  - The optimization of corticosteroids or dopamine antagonists in acute therapy may prevent the need for rescue therapy and may enhance prior regimens in refractory episodes.
  - Highly emetic CINV triple therapy includes steroid, 5HT3, and aprepitant.
  - Agents available for single or combination therapy include *chlorpromazine, prochlorperazine, methylprednisolone, lorazepam, metoclopramide, dexamethasone, haloperidol, and dronabinol.*[1]
  - Note: 5HT3 as a class can cause QT interval prolongation

- Pharmacologic **(RINV)**

  - Many patients will not require treatment and episodes are not as severe or predictable as in CINV.
  - First-line use of 5HT3 in adults and children should be used on each day of radiation therapy. Limited or no evidence supports treatment beyond 24 hours of last radiation dose.
  - Agents used for established RINV include prochlorperazine, metoclopramide, thiethylperazine, chlorpromazine and lorazepam.

- Pharmacologic **(PONV)**
  - High risk patients require prophylactic treatment or multi-modal therapy[3]
  - **Dexamethasone in combination therapy; cost-effective for high risk.[8]
  - Potential treatment with oxygen, ginger, acupressure, and scopolamine.

Standard Dosage for PONV[1]		
Agent (s)	**Dosage (Prophylaxis)**	
	Adult	**Child (20 kg)**
Droperidol**	0.625mg - 1.25mg I.V. q 5 min. (prior to end of anesthesia)	0.015-0.075mg/kg/dose I.V.
Ondansetron	4mg I.V. prior to anesthesia; 8mg P.O. prior to anesthesia	0.05mg/kg I.V. (range, 0.05-0.15mg/kg)
Dolasetron	12.5mg I.V. during operation; 100mg P.O. 1 hr prior to anesthesia	> 2 yr old: 1.8mg/kg I.V. prior to anesthesia
Metoclopramide	10mg - 20mg I.V. (prior to end of operation)	N/A
Promethazine	25mg P.O. 1 hr prior to anesthesia; 12.5 - 25mg I.V. prior to anesthesia	N/A
Prochlorperazine	5 -15mg P.O. 1 hr prior to anesthesia; 5 - 10mg I.M. 1 - 2 hr prior to anesthesia, may repeat 1x in 30 min	N/A
Granisetron	20 - 40mcg/kg I.V.	N/A
	Dosage (Treatment)	
Ondansetron	1 - 4mg I.V. Post-Op	0.05mg/kg/dose I.V.
Metoclopramide	10mg I.V. q 4 - 6 hr prn Post-Op	N/A
Promethazine	10 - 25mg P.O. q 4 - 6 hr prn Post-Op; 12.5 - 25mg I.V. or I.M. q 4 h prn Post-Op	N/A
Prochlorperazine	5 - 15mg P.O. Post-Op; 5 - 10mg I.M. , may repeat once in 30 min.; 5 - 10mg I.V., may repeat once	N/A
Chlorpromazine	10 - 25mg P.O. q 4 - 6 hr prn; 12.5 - 25mg I.M. if no hypotension; may repeat in 1 hr prn	0.55mg/kg P.O. or I.M.
Droperidol	0.625 - 0.125mg I.V. prn	0.1mg/kg/dose I.V.
Dolasetron	12.5mg I.V. Post-Op	N/A
Propofol	20mg P.O. bolus Post-Op	

- Pharmacologic **(Nausea and Vomiting in Pregnancy)**
  - Ginger is found to significantly improve symptoms of NVP and hyperemesis gravidarum at 250 mg four times daily.[2]
  - Pyridoxine 10-25 mg every eight hours on an intermittent basis of 2 to 3 day intervals.[2]
  - Doxylamine (Unisom) 12.5 mg in combination with pyridoxine up to 3 times a day.[2]
  - Potential treatment with diphenhydramine, mirtazapine, or dimenhydrinate.[2]
  - Promethazine P.O., I.V., or I.M. 12.5-25 mg every 4-6 hours as needed.[4]
  - Metoclopramide 20 to 40 mg P.O. q 4 to 6 h prn.[9]

Cost and Utilization

For the period of July 2004 through June 2005, a total of 8,085 members received antiemetic products through the SoonerCare program.

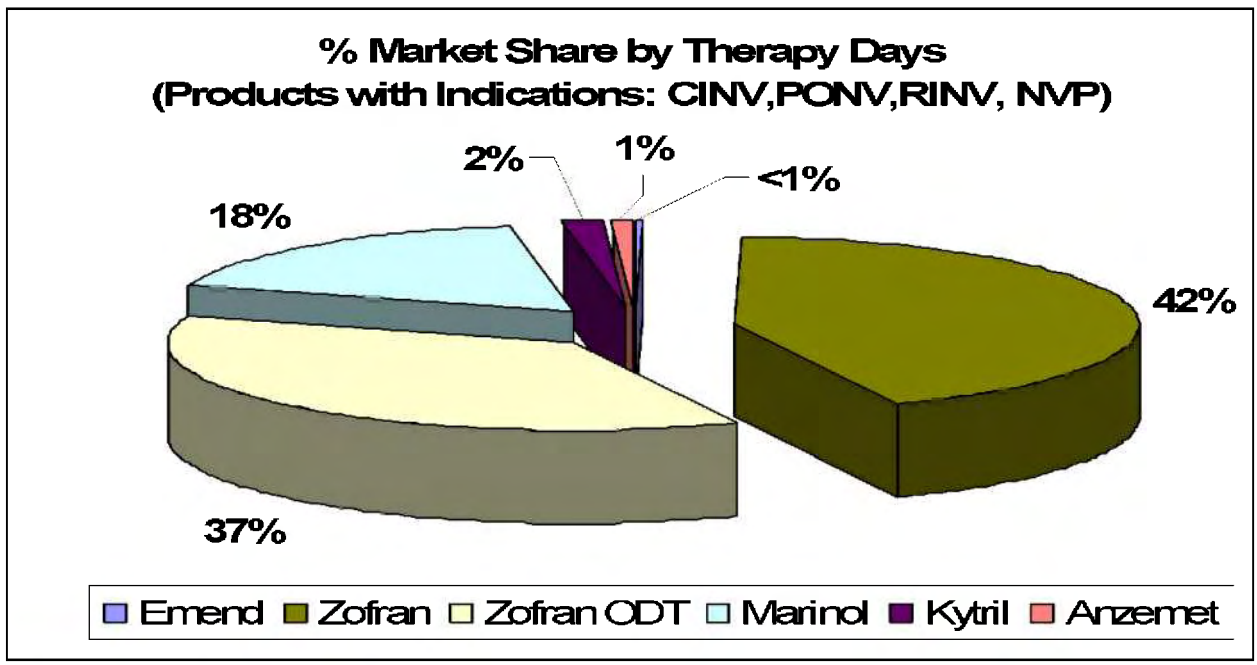
FY 2004 versus FY 2005			% Change
Cost FY '05		**$ 2,255,605.12**	**10.4 ↑**
	Cost FY '04	*$ 2,043,151.24*	
Claims FY '05		**19,932**	**37.8 ↑**
	Claims FY '04	*14,460*	
Cost per Claim FY '05		**$ 113.17**	**20 ↓**
	Cost per Claim FY '04	*$141.30*	
Members FY '05		**8,085**	**46.2 ↑**
	Members FY '04	5,531	

Anti-emetic Products*	Total Units	Total Days	Units per day	Total Cost	Per Diem	% change (Cost FY '04)
Antidopaminergic	45	13	3.5	33.50	$2.50	8.7 ↑
Anticholinergic	29,927	53,132	0.6	139,737.92	$2.63	57.1↑
Antihistaminic	752,896	249,956	3.0	73,443.68	$0.29	23.5 ↑
Cannabinoids	48,741	22,695	2.2	332,300.93	$14.64	44.0 ↑
5-HT3 Antagonists	79,210	106,120	0.8	1,694,259.51	$15.97	2.2 ↑
Substance P Antagonist	168	237	0.7	15,829.58	$66.80	151 ↑

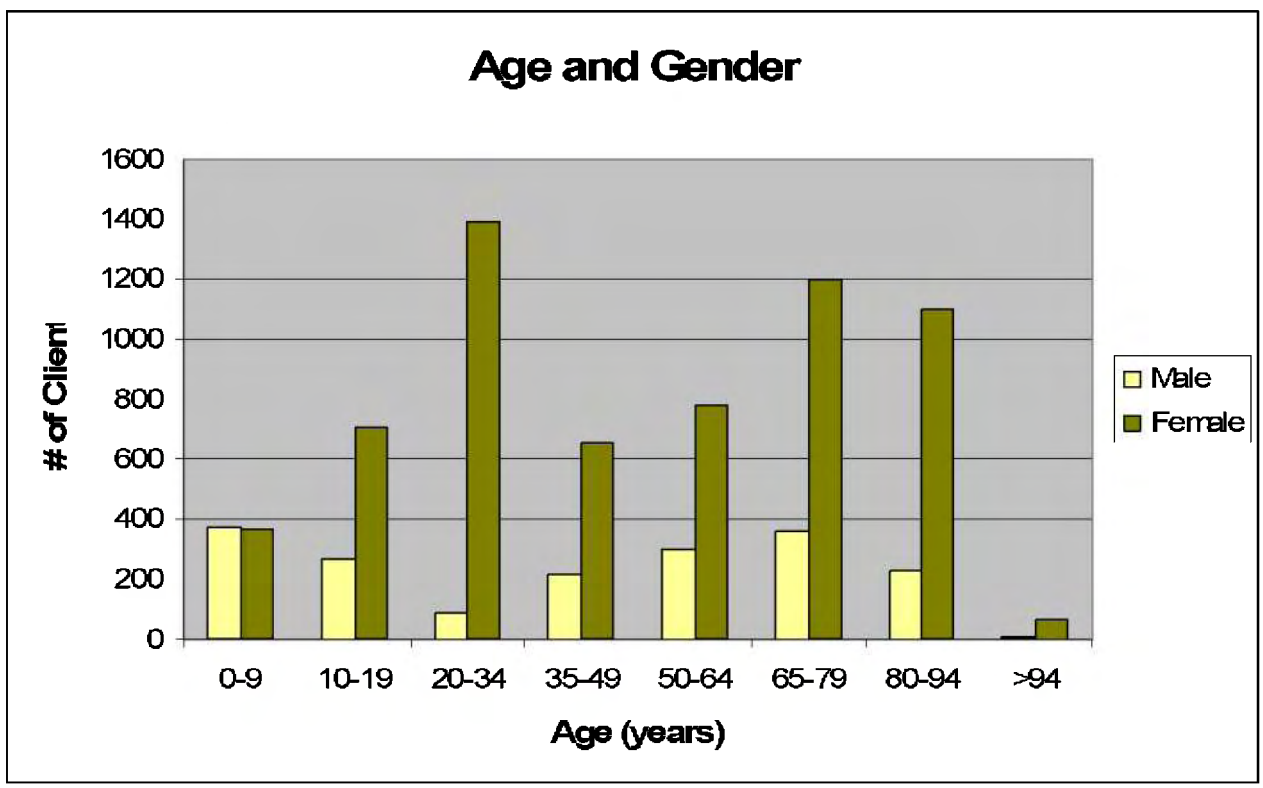
*excludes prokinetic (metoclopramide) and anti-psychotic (prochlorperazine)

Fiscal year 2005, the 5HT3 receptor antagonists accounted for only 25% of claims but incurred 75% of the cost. Quantity limits of 12 tablets per 30 days were implemented in June 2004 for 5HT3 antagonist Zofran®. Quantities exceeding monthly limit may be considered for approval with quantity limit override request.

Market Share of 5HT3 Antagonists, Substance P Antagonist, and Marinol



Age and Gender FY '05 Members on Antiemetics

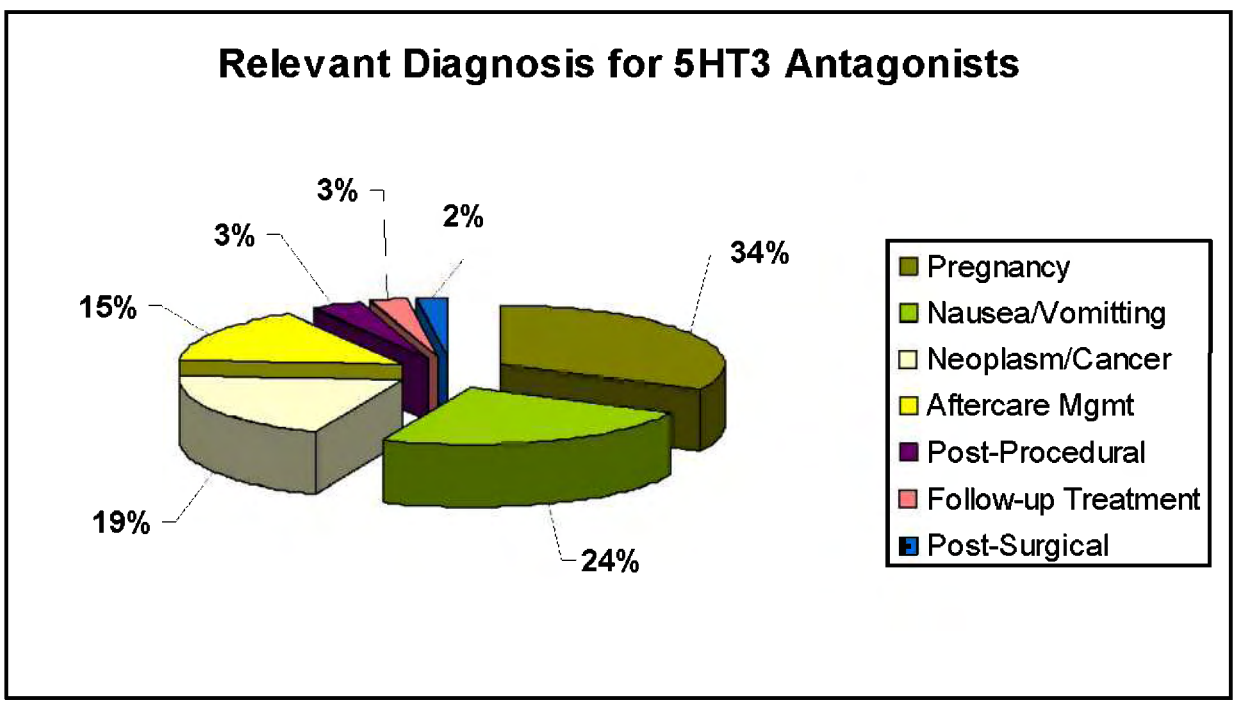


Dual and Non-Dual Eligible Members

FY 2005	# of Members	# of Claims	Total Units	Total Days	Total Cost	Per Diem
Duals	3,820	11,879	689,005	270,544	$611,759.35	$2.26
Non-Duals	4,265	8,053	221,982	161,609	$1,643,845.77	$10.17

Relevant Diagnoses Analysis with 5HT3 Antagonists

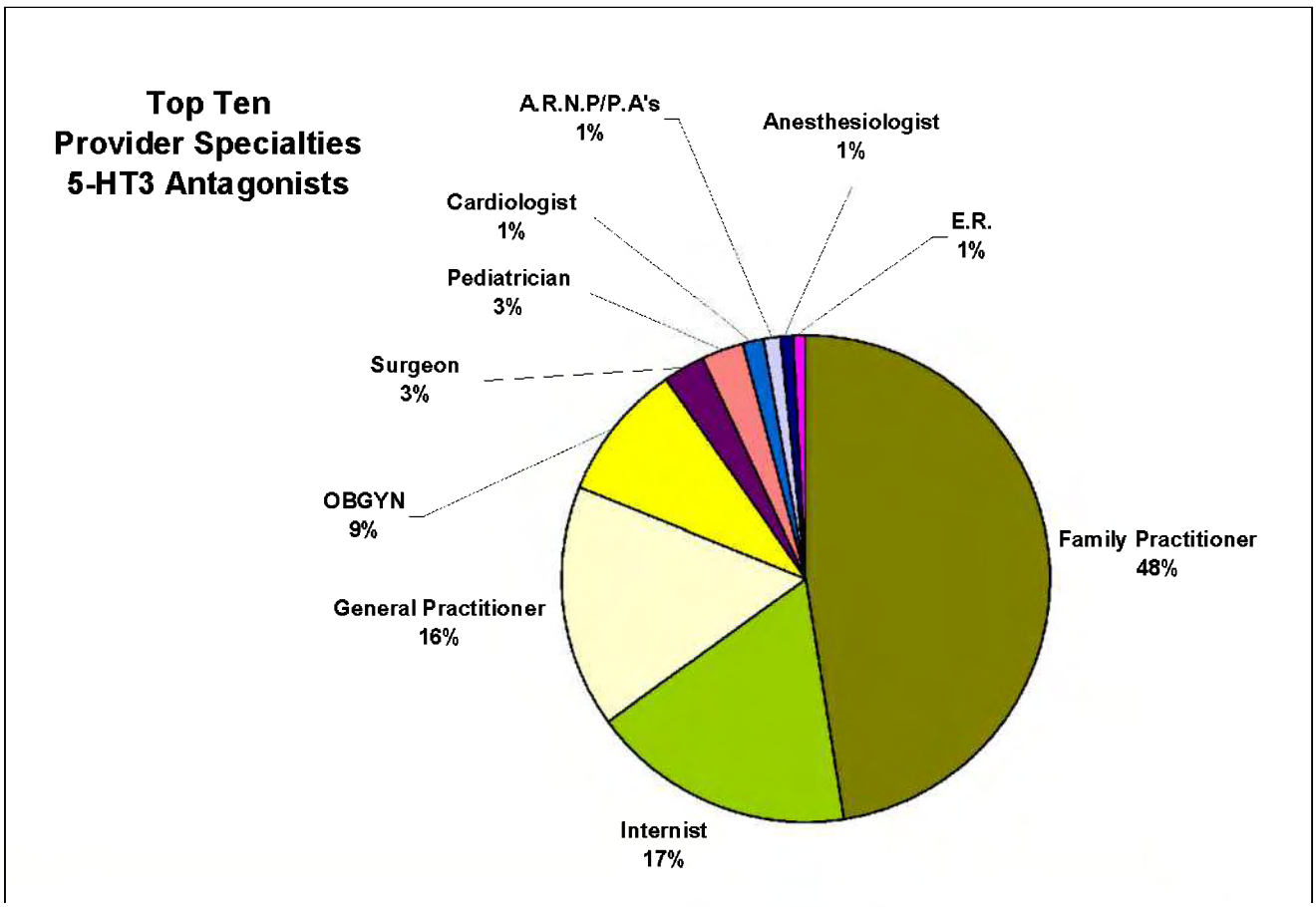
The 5HT3 antagonists are FDA approved for use in CINV, RINV, and PONV. Analysis of medical and hospital claims of members who had claims of 5HT3 antagonists was conducted to assess appropriate use of antiemetics by relevant ICD-9 diagnoses.



The high cost of select groups of antiemetics has led to the development of consensus guidelines which have been implemented in many hospitals and clinics to assist in appropriate cost-effective management of nausea and vomiting according to patient risk factors and evidence based medicine.

Prescriber Specialty

Lack of consistency in prescribing and adherence to consensus guidelines can have a substantial impact on quality of care and unnecessary medical costs.



Conclusion

- ✓ Nausea and vomiting is a common occurrence which may be acute or chronic in nature depending on etiology and individual risk factors.
- ✓ Prevention is vital due to difficulty of treating established nausea and vomiting.
- ✓ Adequate assessment of nausea and vomiting risk factors are necessary when selecting either non-pharmacologic or pharmacologic therapies.
- ✓ Lack of consistent prescribing can yield inadequate or inappropriate use of anti-emetics and unnecessary medical costs due to rescue therapy, wasted drug, or hospital/E.R. visits.
- ✓ Complex involvement of neurotransmitters, receptors, physiologic injury, infectious disease, learned behavioral response, gastrointestinal obstruction, or exposure to emetogenic substances may require multi-modal therapy.
- ✓ Side-effect profiles and costs guide medical therapy selection.
- ✓ 5HT3 antagonists do not significantly differ in efficacy in regards to oral versus I.V.[6]
- ✓ Lack of initial response may require increased dose, addition of agent, or change in pharmacologic class.

Update on Market News

January 2005 – Wyeth Pharmaceuticals issued "Dear Healthcare Professional" letter reinforcing the black box warning in use of promethazine in children less than two years of age.
November 2005 – Marinol® was changed from Schedule II to Schedule III in Oklahoma.[11]
December 2006 – Patent expiration on Zofran® products.[12]

Recommendation

The College of Pharmacy recommends consideration of product based prior authorization for 5HT3 antagonists, substance P antagonists, and cannabinoids to ensure appropriate utilization. Quantity limits already established will remain unchanged.

Purpose: Ensure appropriate utilization of antiemetic medication.

Why: Antiemetic prescription claims accounted for 19,932 prescription drug claims, totaling $2,255,605.12, for the period of July 01,2004 thru June 30,2005. The 5HT3 receptor antagonists accounted for only 25% of claims but incurred 75% of the cost. Analysis of relevant ICD-9 diagnosis indicates about 34% of members using 5HT3 antagonists had a diagnosis of pregnancy and 24% for non-specific nausea and vomiting. Due to the shift to coverage for non-dual members, the use of these medications for non-oncology related diagnoses is expected to increase. In addition, aprepitant is approved only in combination with other antiemetic medications. Dronabinol should only be used as a third-line antiemetic agent.

Anti-emetic Products*	Total Units	Total Days	Units per day	Total Cost	Per Diem	% change (Cost FY '04)
Antidopaminergic	45	13	3.5	33.50	$2.50	8.7 ↑
Anticholinergic	29,927	53,132	0.6	139,737.92	**$2.63**	57.1↑
Antihistaminic	752,896	249,956	3.0	73,443.68	$0.29	23.5 ↑
Cannabinoids	48,741	22,695	2.2	332,300.93	$14.64	44.0 ↑
5-HT3 Antagonists	79,210	106,120	0.8	1,694,259.51	$15.97	2.2 ↑
Substance P Antagonist	168	237	0.7	15,829.58	$66.80	151 ↑

*excludes prokinetic (metoclopramide) and anti-psychotic (prochlorperazine)

Criteria would be as follows:

1. *First 30 days of therapy available without a PA.*
2. *Further approval beyond initial 30 days of therapy will require FDA approved diagnosis and clinical supporting information on failure or contraindication with at least TWO conventional antiemetic drug therapies at maximum FDA approved daily dose with dates and dosages.*

Clinical Exceptions:

1. *Approvals granted for members undergoing chemotherapy, radiation therapy or surgery for cancer related diagnosis under the supervision of oncologist.*
2. *Documented adverse effect, drug interaction, or contraindication to tier-1 products.*
3. *Approvals granted for hyperemesis gravidarum with supporting documentation of week of gestation, presence of weight loss, recent hospitalizations or emergency room visits due to hyperemesis, or history of hyperemesis gravidarum with previous pregnancies.*
4. *Approval of tier-2 medication if there is a unique FDA-approved indication not covered by any tier-1 products.*

Due to uniqueness of side-effects, efficacy, and costs, appropriate management and cost-effective use of antiemetics in nausea and vomiting have the potential to improve quality of life while reducing unnecessary medical costs.

Antiemetic Medications*	
Tier 1	**Tier 2**
Dexamethasone, methylprednisone, cortisone, prednisone, prednisolone	Dolasetron
Torecan	Granisetron
Meclizine, hydroxyzine	Palonosetron
Promethazine, prochlorperazine, chlorpromazine	Dronabinol
Scopolamine, trimethobenzamide,	Ondansetron
Metoclopramide	Aprepitant (only in combination with corticosteroid or 5HT3 antagonist)
Droperidol	

* All versions of the prescription only product will remain Tier 2 until a SMAC can be applied or a supplemental rebate is established.

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APPENDIX E

Drug Utilization Review of Antibiotics and Related Products

Oklahoma HealthCare Authority

April 2006

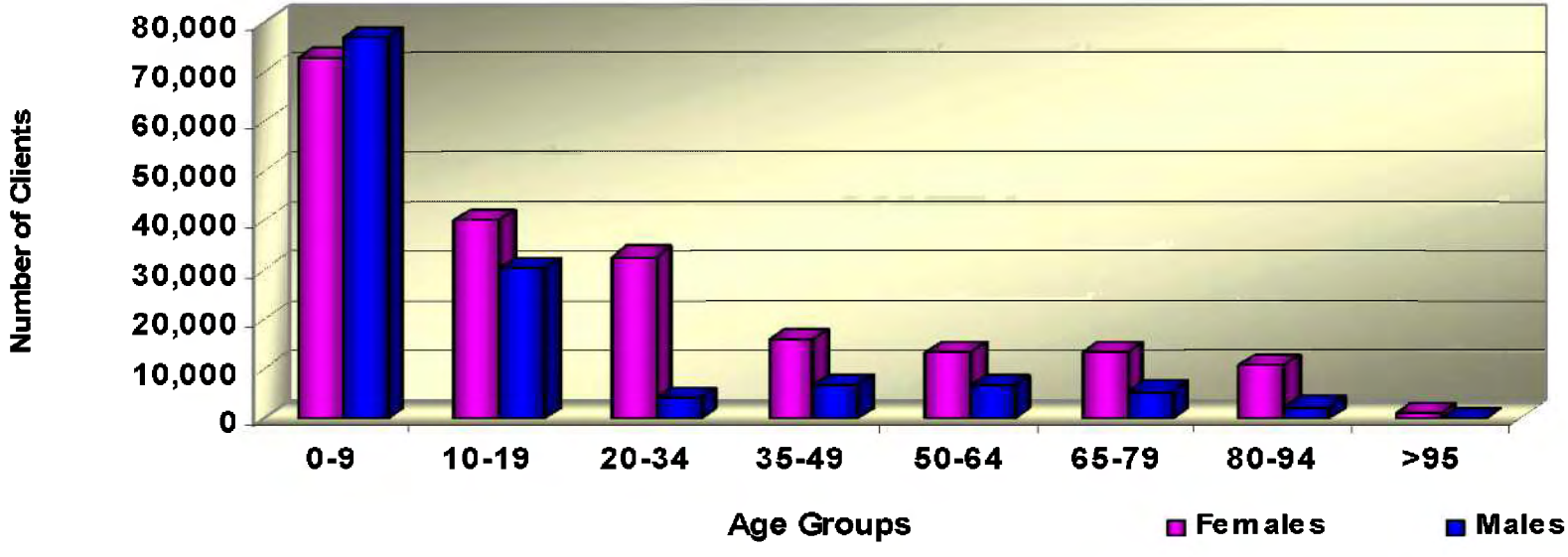
For the period of January 2005 through December 2005, a total of 331,875 members received antibiotics and related products through the Oklahoma HealthCare Authority Pharmacy program. (Attachment A has a list of common drugs in each class)

DRUGNAME	CLAIMS	UNITS	DAYS	COST	Cost/Claim	% Cost	% Claims
1. Penicillin	21,350	1,400,802	201,783	$206,931.73	$9.69	0.49%	2.45%
2. Ampicillins	190,101	19,979,483	1,841,252	$1,574,835.21	$8.28	3.72%	21.86%
3. Extended Spectrum	22	1,150	205	$2,744.29	$124.74	0.01%	0.00%
4. Penicillin Combos	68,726	6,572,491	694,915	$3,881,733.66	$56.48	9.16%	7.90%
5. Penicillinase Resistent	1,223	73,890	12,301	$67,916.00	$55.53	0.16%	0.14%
6. 1st Gen. Cephs	77,751	5,080,389	728,001	$1,160,178.61	$14.92	2.74%	8.94%
7. 2nd Gen. Cephs	30,001	2,433,728	295,404	$1,647,821.06	$54.93	3.89%	3.45%
8. 3rd Gen. Cephs	37,211	2,431,367	355,309	$3,379,698.31	$90.83	7.98%	4.28%
9. 4th Gen. Cephs	90	9,421	550	$31,445.32	$349.39	0.07%	0.01%
10. Macrolides	168,108	3,089,365	941,770	$7,374,184.91	$43.87	17.40%	19.33%
11. Tetracyclines	29,036	1,029,170	561,171	$588,873.19	$20.28	1.39%	3.34%
12. Fluoroquinolones	61,129	892,203	527,061	$3,541,443.52	$57.93	8.36%	7.03%
13. Aminoglycosides	1,565	292,984	25,426	1,280,078.94	$817.94	3.02%	0.18%
14. Antimycobacterials	1,414	55,817	28,427	$94,702.48	$66.97	0.22%	0.16%
15. Antifungals	31,175	1,385,409	413,608	$2,181,399.76	$69.97	5.15%	3.58%
16. Antiretrovirals	13,747	1,122,909	419,728	$7,376,040.56	$536.56	17.41%	1.58%
17. CMV Agents	300	32,079	8,547	$483,796.40	$1,612.65	1.14%	0.03%
18. Hep C Agents	1,966	138,219	58,698	$2,685,180.93	$1,365.81	6.34%	0.23%
19. Herpes Agents	10,499	578,876	166,347	$826,656.42	$78.74	1.95%	1.21%
20. Influenza A	3,830	101,660	23,087	$232,398.31	$60.68	0.55%	0.44%
21. Antimalarials	15,126	763,413	566,032	$231,073.06	$15.28	0.55%	1.74%
22. Misc. Anti-infectives	101,762	7,223,851	1,149,786	$3,436,087.30	$33.77	8.11%	11.70%
23. Vaccines	3,617	2,202	9,259	$91,071.49	$25.18	0.21%	0.42%
Totals	**869,749**	**54,690,878**	**9,028,667**	**$42,376,291.46**	**$48.72**	**100.00%**	**100.00%**

Top 10 Classes by Number of Members and Cost

Amp	Azith	1st Gen	Pen Comb	Misc Comb	Fluoro	3rd Gen	2nd Gen	Tetra	Pen
132,528	105,610	59,761	52,375	48,479	37,629	27,387	23,430	18,620	16,915
Antiretro	**Azith**	**Pen Comb**	**Fluoro**	**3rd Gen**	**Hep C**	**2nd Gen**	**Amp**	**Antifung**	**Oxazol**
$7.376 M	$6.729 M	$3.881 M	$3.541 M	$3.379 M	$2.685 M	$1.647 M	$1.574 M	$1.425 M	$1.410 M

Demographics of All Members



Groups	Members		Claims		Days		Total Cost
All	**331,875**		**869,749**		**9,028,667**		**$ 42,376,291.46**
NonDuals	**(84 %) 279,774**	**(79 %)**	**687,465**	**(74 %)**	**6,679,592**	**(68 %)**	**$ 28,853,386.40**
Duals	**(16 %) 52,101**	**(21 %)**	**182,284**	**(26 %)**	**2,349,075**	**(32 %)**	**$ 13,522,905.06**

Trends in Utilization

	Calendar Year 2004	Calendar Year 2005	Percent Change	
Total Cost	**$ 37,552,495.15**	**$ 42,376,291.46**	**Increased**	**12.8 %**
Total Claims	**745,235**	**869,749**	**Increased**	**16.7 %**
Cost/Claim	**$ 50.40**	**$ 48.72**	**Decreased**	**3.33 %**

Class	Cost			Claims		
	CY 2004	CY 2005	% Change	CY 2004	CY 2005	% Change
1. Penicillin	$ 194,544.37	$ 206,931.73	**6.37**	19,489	21,350	**9.55**
2. Ampicillins	$ 1,474,805.99	$ 1,574,835.21	**6.78**	164,747	190,101	**15.39**
3. Extended Spectrum	$ 10,136.56	$ 2,744.29	**-72.93**	44	22	**-50.00**
4. Pen Combos	$ 4,179,560.50	$ 3,881,733.66	**-7.13**	63,692	68,726	**7.90**
5. Pen Resistent	$ 61,352.09	$ 67,916.00	**10.70**	1,341	1,223	**-8.80**
6. 1st Gen. Cephs	$ 1,251,750.45	$ 1,160,178.61	**-7.32**	78,395	77,751	**-0.82**
7. 2nd Gen. Cephs	$ 1,546,553.54	$ 1,647,821.06	**6.55**	28,473	30,001	**5.37**
8. 3rd Gen. Cephs	$ 2,087,704.67	$ 3,379,698.31	**61.89**	24,664	37,211	**50.87**
9. 4th Gen. Cephs	$ 48,750.12	$ 31,445.32	**-35.50**	160	90	**-43.75**
10. Macrolides	$ 5,852,016.01	$ 7,374,184.91	**26.01**	137,911	168,108	**21.90**
11. Tetracyclines	$ 491,481.41	$ 588,873.19	**19.82**	25,247	29,036	**15.01**
12. Fluoroquinolones	$ 3,734,015.81	$ 3,541,443.52	**-5.16**	51,814	61,129	**17.98**
13. Aminoglycosides	$ 1,252,972.83	$ 1,280,078.94	**2.16**	1,438	1,565	**8.83**
14. Antimycobacterials	$ 63,826.17	$ 94,702.48	**48.38**	907	1,414	**55.90**
15. Antifungals	$ 2,538,989.99	$ 2,181,399.76	**-14.08**	28,076	31,175	**11.04**
16. Antiretrovirals	$ 5,967,233.68	$ 7,376,040.56	**23.61**	12,320	13,747	**11.58**
17. CMV Agents	$ 415,062.75	$ 483,796.40	**16.56**	269	300	**11.52**
18. Hep C Agents	$ 2,995,731.90	$ 2,685,180.93	**-10.37**	2,173	1,966	**-9.53**
19. Herpes Agents	$ 645,751.53	$ 826,656.42	**28.01**	8,872	10,499	**18.34**
20. Influenza A	$ 49,209.01	$ 232,398.31	**372.27**	841	3,830	**355.41**
21. Antimalarials	$ 255,898.52	$ 231,073.06	**-9.70**	13,385	15,126	**13.01**
22. Misc. Anti-infectives	$ 2,384,044.30	$ 3,436,087.30	**44.13**	79,696	101,762	**27.69**
23. Vaccines	$ 51,102.76	$ 91,071.49	**78.21**	1,281	3,617	**182.36**
Totals	**$ 37,552,494.96**	**$ 42,376,291.46**	**12.85**	**745,235**	**869,749**	**16.71**

Conclusion and Recommendations

The College of Pharmacy recommends further review of the classes listed below and other classes as suggested by the Drug Utilization Review Board.

- Ampicillin
- Penicillin Combos
- 3rd Generation Cephalosporins
- Macrolides (Azithromycin)
- Fluoroquinolones
- Influenza A Agents
- Oxazolidinedione

Attachment A

Classes and Common Drugs by Claims

1. Penicillin
Pen VK 500 and 250mg
Veetids Sol
Pen G Inj

2. Ampicillins
Trimox Susp and Caps
Amoxil Susp and Caps
Ampicillin Inj

3. Extended Spectrum - Geocillin

4. Pen Combos
Augmentin Susp and Tabs
Unisyn, Timentin, Zosyn Inj

5. Pencnase-Resistent
Diclox, Nafcillin, Oxacillin

6. 1st Gen Cephalosporins
Cephalexin Caps, Tabs, Susp
Duricef Susp
Cefadroxil

7. 2nd Gen Cephalosporins
Cefzil Susp, Tabs
Cefaclor Susp, Caps
Cefuroxime Susp, Tabs

8. 3rd Gen Cephalosporins
Omnicef Susp, Caps
Rocephin Inj
Vantin Susp, Tabs
Cedax Susp, Fortaz, Tazicef

9. 4th Gen Cephalosporins
Maxipime

10. Macrolides
Ery-Tab, EES Susp
Zithromax Susp 200/5, Z-pack
Biaxin 500, XL 500mg

11. Tetracyclines
Doxy 100, Caps, Tabs
Mino Caps
Tetra Caps

12. Fluoroquinolones
Levaquin
Cipro 500, XR 500
Tequin, Avelox

13. Aminoglycosides
Tobi Neb
Neomycin Tab
Gentamycin Inj

14. Antimycobacterials
Rifampin Cap 300, 150
Ethambutol
Isoniazid

15. Antifungals
Grifulvin V Susp and Tab
Lamisil Tab 250
Gris-Peg Tab 250

15. Antifungal-Imidazole
Fluconazole Tab and Susp
Sporanox
Ketoconazole

15. Antifungal-Glucan Synth Inh
Cancidas, Mycamine Inj

16. Antiretrovirals
Kaletra, Combivir, Sustiva
Truvada, Norvir, Epivir

17. CMV Agents
Valcyte
Cytovene, Ganciclovir, Foscavir

18. Hep C Agents
Pegasys Kit
Ribavirin Cap, Tabs
Peg-Intron Kit

19. Herpes
Acyclovir Caps, Tabs, Susp
Valtrex, Famvir

20. Influenza A
Tamiflu Caps, Susp
Rimantadine, Fluma, Relenza

21.Antimalarials
Quinine Sulf. Caps, Tab
Plaquenil
Malaril

22. Miscellaneous
Vermox
Metronidazole 500
Trimethoprim 100
Vancomycin Inj
Polymyxin B
Primaxin, Merrem, Ivanz
Gantris Susp, Sulfadiazine Tab
Clindamycin, Lincocin
Oxazolidinedione-Zyvox
Dapsone, Lamprene
Alinia, Mepron
TMP/SMZ Tabs, Susp
EES/Sulfasox Susp

23. Viral Vaccines
Fluzone Inj.
Fluvirin Inj.
Vaqta Inj.

23. Bacterial Vaccines
Pnu-Immune Inj.
Menomune Inj.

APPENDIX F

Review of Contraceptive Utilization

Oklahoma Health Care Authority
April 2006

Introduction

Contraception products use various combinations of estrogen and progesterone in monthly fixed or varying doses to prevent ovulation. Estrogen components include ethinyl estradiol and mestranol; progesterone components include levonorgestrel, desogestrel, norethindrone, norgestrel, ethynodiol, norgestimate, and drospirenone. Dosing can be monophasic, biphasic, or triphasic. Contraception can also be achieved using progestin only (norethindrone or medroxyprogesterone). Alternative delivery systems include intramuscular or subcutaneous injection, transdermal patch, vaginal ring, or intrauterine device (IUD).

Indications

FDA approved indications

- Contraception
- Postcoital contraception
- Hypermenorrhea
- Acne

Off-label uses

- Dysmenorrhea
- Dysfunctional uterine bleeding
- Endometriosis
- Polycystic Ovary Syndrome
- Hirsutism
- Perimenopausal symptoms

Precautions

- Pregnancy
- Active liver disease
- Breast cancer
- Endometrial cancer
- Estrogen dependent cancer
- Hepatic cancer
- Thromboembolic disorders (active/history)
- Smokers >35/heavy smokers
- CAD
- Cardiovascular disease
- Diabetes w/ vascular disease
- Hypertension

Utilization

From January through December 2005 a total of 24,563 members used a contraceptive product through the Oklahoma SoonerCare program.

Comparison		% Change
Total Cost CY '05	**$3,657,841.99**	**11.6↑**
Total Cost CY '04	*$3,277,796.84*	
Total Claims CY '05	**77,952**	**6.8↑**
Total Claims CY '04	*72,963*	
Total Members CY '05	**24,563**	**6.2↑**
Total Members CY '04	*23,127*	
Per Diem CY '05	**$1.29**	**0.8↑**
Per Diem CY '04	*$1.28*	

Oral Contraceptives

Drug	Claims	Units	Days	Members	Cost	$/month*
Camila 0.35 mg	1,024	35,054	35,010	575	$42,322.46	$33.80
Errin 0.35 mg	2,355	83,414	83,080	1,339	$99,394.74	$33.36
Jolivette 0.35 mg	344	11,004	10,943	181	$13,373.32	$34.03
Nor-QD 0.35 mg	194	8,390	9,024	137	$13,522.76	$45.07
Nora-BE 0.35 mg	270	11,152	10,787	169	$12,782.26	$32.12
Ortho Micron dialpak	161	5,854	5,886	109	$10,742.41	$51.40
Ovrette 28 0.075 mg	8	280	280	6	$369.21	$36.92
Apri tab	559	20,692	20,228	156	$17,933.41	$24.27
Desogen-28	40	1,652	1,599	21	$1,876.42	$31.80
Ortho-Cept 28	9	504	478	6	$834.89	$46.38
Reclipsen tab	8	280	280	6	$251.61	$25.16
Solia tab	71	2,464	2,431	23	$2,172.71	$24.69
Kariva tab 28	895	31,192	30,720	243	$32,134.16	$28.84
Mircette tab 28	103	3,416	3,353	32	$4,442.61	$36.41
Yasmin 3.0-0.03mg	6,445	215,985	216,434	2,067	$314,875.08	$40.82
Demulen 1/35-21	1	28	28	1	$42.84	$42.84
Demulen 1/35-28	41	1,680	1,582	13	$2,178.65	$36.31
Kelnor 1/35	7	196	154	2	$213.08	$30.44
Zovia 1/35E	291	9,380	9,331	76	$9,641.72	$28.78
Demulen 1/50-28	14	868	854	5	$1,227.87	$39.61
Zovia 1/50E	74	2,296	2,296	15	$2,644.08	$32.24
Alesse tab-28	283	9,212	9,208	102	$12,119.58	$36.84
Aviane tab	1,639	54,264	54,274	531	$55,684.89	$28.73
Lessina-28	773	26,628	26,450	231	$28,628.31	$30.10
Levlite-28	285	8,348	8,396	109	$10,821.02	$36.31
Lutera tab	99	3,000	3,100	40	$3,158.06	$29.51
Levlen tab	699	35,105	35,774	280	$42,383.75	$33.80
Levora-28 0.15/30	795	24,640	24,251	207	$24,427.46	$27.76
Nordette-28	37	1,204	1,210	22	$1,725.78	$40.13
Portia-28	300	9,772	9,592	87	$10,426.47	$29.87
Ovcon-35 21 tabs	1	84	84	1	$123.76	$30.94
Ovcon-35 28 tabs	1188	42,180	42,359	548	$62,539.69	$41.53
Brevicon 0.5/35	17	532	532	3	$606.71	$31.93
Modicon 0.5/35-28**	2	56	56	1	$30.92	$15.46
Necon 0.5/35	14	392	392	7	$426.51	$30.46
Nortrel 28	15	1,064	1,064	7	$1,051.30	$27.66
Necon 1/35-21**	3	252	168	2	$205.65	$17.14
Necon1/35-28	1,358	44,856	43,673	418	$40,377.97	$25.20
Norethrin 1/35**	1	28	28	1	$13.00	$13.00
Norinyl 1+35-28	406	17,541	17,672	195	$15,471.68	$24.68
Notrel 1/35 28	992	33,015	32,709	283	$29,926.51	$25.38
Ortho-Novum 1/25-28	21	644	650	9	$642.47	$27.93
Ovcon 50 28	201	6,664	6,233	61	$10,868.97	$45.67
Junel 1/20 - 21	9	364	364	6	$459.71	$25.54
Loestrin 1/20-21	10	618	645	6	$1,273.54	$42.45
Microgestin1/20 -21	33	1,050	1,043	15	$1,359.59	$27.19
Junel 1.5/30 -21	8	469	469	5	$601.97	$27.36
Loestrin-21 1.5/30	10	252	252	2	$555.18	$46.27
Microgestin 1.5/30	30	1,519	1,582	13	$1,934.97	$26.15
Necon 1/50-21	3	84	84	1	$116.19	$29.05
Necon 1/50-28	271	10,486	9,868	110	$10,495.51	$27.99

Drug	Claims	Units	Days	Members	Cost	$/month*
Norinyl 1+50-28	59	2,460	2,381	22	$3,310.43	$37.62
Ortho-Novum 1/50-28	33	1,344	1,326	11	$2,240.92	$46.69
Cryselle-28	741	24,528	24,065	209	$25,443.43	$29.04
Lo/Ovral	297	9,884	9,744	102	$12,714.77	$36.02
Low-Ogestrel	1,120	37,520	37,101	336	$39,196.28	$29.25
Ogestrel	197	5,799	5,356	55	$8,939.75	$43.19
Ovral-28	19	532	532	6	$1,041.20	$54.80
Mononessa	315	9,240	9,166	99	$10,555.41	$31.99
Ortho-Cyclen 0.25/35	230	7,840	7,853	74	$12,302.86	$43.94
Previfem tab	11	364	364	4	$370.21	$26.17
Sprintec 28	2,408	76,608	76,081	789	$78,809.05	$28.80
Junel Fe 1/20	273	9,268	8,983	77	$8,014.32	$24.21
Loestrin Fe 1/20	122	6,020	6,002	56	$9,201.88	$42.80
Microgestin Fe 1/20	257	8,988	8,671	76	$8,833.57	$27.52
Junel Fe 1.5-30	193	6,552	6,458	70	$5,719.68	$24.44
Loestrin Fe 1.5/30	78	2,520	2,464	19	$3,999.94	$44.44
Microgestin Fe 1.5/30	215	7,056	6,911	61	$7,102.34	$28.18
Necon 10/11-28	27	896	896	9	$1,001.20	$31.29
Ortho-Novum 10/11-28	7	252	252	3	$453.96	$50.44
Cesia Pak	20	616	616	6	$694.18	$31.55
Cyclessa Pak	89	2,884	2,866	28	$4,003.68	$38.87
Velivet Pak	297	10,360	10,340	77	$10,494.98	$28.36
Enpresse-28	693	22,709	22,368	158	$21,392.01	$26.38
Tri-Levlen 28	584	26,553	26,794	245	$31,571.27	$33.30
Triphasil 21	6	126	126	1	$185.46	$30.91
Triphasil 28	248	8,092	8,071	73	$9,993.14	$34.58
Trivora-28	874	28,924	28,918	242	$25,604.35	$24.79
Necon 7/7/7 28 day	679	25,697	25,597	220	$26,759.21	$29.15
Nortrel 7/7/7 28 day	532	19,150	19,065	140	$19,053.42	$27.86
Ortho-Novum 7/7/7 -28	135	6,726	6,766	82	$9,998.70	$41.66
Aranelle tab	20	728	728	4	$943.07	$36.27
Leena tab	1	28	30	1	$38.78	$38.78
Tri-Norinyl 28	10	338	284	9	$528.45	$44.04
Ortho-Tri-Cyclen Lo	6,434	216,498	216,258	2,279	$322,864.77	$41.76
Ortho-Tri-Cyclen	1,039	34,362	34,202	359	$49,450.04	$40.30
Tri-Previfem	160	5,908	5,908	65	$7,073.34	$33.52
Tri-Sprintec	3,680	120,514	119,939	1,283	$139,777.85	$32.48
Trinessa	6,332	208,502	209,273	2,158	$235,802.51	$31.66
Estrostep Fe	710	24,164	24,018	298	$35,621.55	$41.28
Seasonale	1,141	103,595	100,432	690	$150,667.46	$40.72
TOTALS	**52,703**	**1,864,951**	**1,853,165**	**16,435***	**$2,293,202.83**	**$29.85**

*Unduplicated members
** Cost based on 28 day month.
*** Obsolete NDC

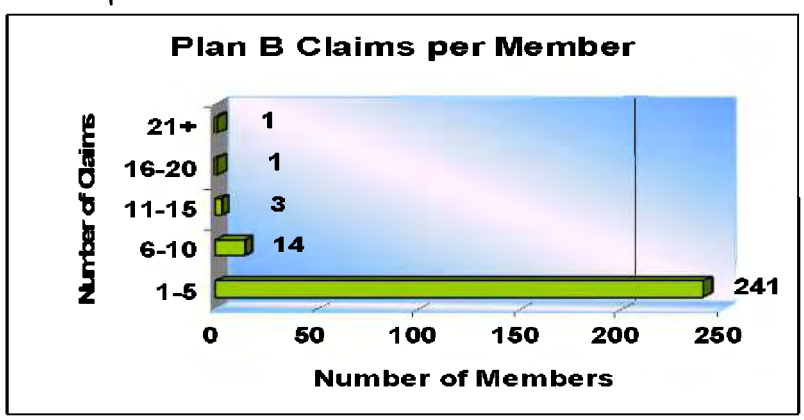
Other contraceptive delivery systems

Drug	Claims	Units	Days	Members	Cost	$/unit	$/month
Depo-Provera 150 mg/ml	3,303	3,622	190,440	1,931	$205,843.59	$56.83	$30.26
Medroxyprogesterone 150 mg/ml	3,725	4,216	239,082	2,243	$207,898.84	$49.31	$24.35
Depo-SQ Provera	7	9	475	7	$781.43	$86.83	$28.94
Mirena IUD System	28	28	1,662	28	$10,826.51	$386.66	$32.22**
Plan B tab 0.75 mg	522	1,044	847	260	$15,131.47	$14.47	$28.94***
Ortho Evra	15,138	56,678	477,015	5,234	$800,707.70	$14.13	$47.00
Nuvaring	2,526	3,146	82,974	1,031	$123,448.62	$39.24	$41.66
TOTAL	**25,249**	**68,743**	**992,495**	**9,690***	**$1,364,639.16**	**$19.85**	**$38.50**

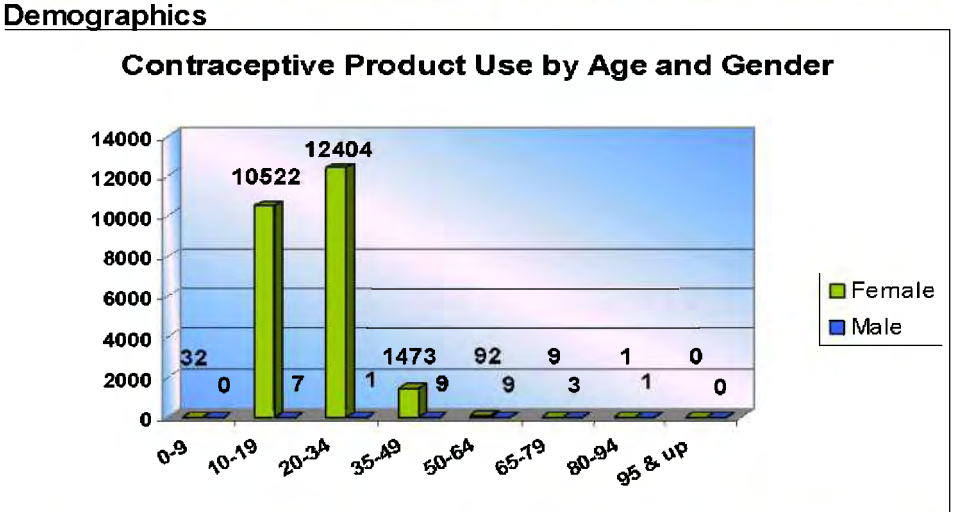
*Unduplicated members
**Can be used up to 5 years, this monthly cost based on 12 months of use.
***Cost per use

Plan B Utilization

Review of Plan B use shows that several members have been using Plan B on a routine basis rather than on an intermittent or emergency basis, or during the first month of oral contraceptives.



Demographics



Diagnostic Evaluation

Thirty (30) male members had claims for contraceptives, primarily medroxyprogesterone. Review of ICD-9 diagnosis codes for 2003 through 2005 revealed that the majority of these members (22) had some type of behavioral diagnosis. Medroxyprogesterone has off-label use for reducing aggressiveness and sexual behavior associated with dementia.

Conclusions

- Prescription and non-prescription contraceptives do not count against a member's script limit.
- Depo-Provera and brand-name oral contraceptives, available in generic and having SMAC pricing applied, can be obtained only by requesting a Brand-Only override.

Recommendations

- The College of Pharmacy recommends continuing to monitor this drug class.
- Provide focused educational information to physicians regarding appropriate use of Plan B.

APPENDIX G

30 Day Notice to Prior Authorize Amitiza™ (lubiprostone)

Oklahoma Health Care Authority
April 2006

Manufacturer Sucampo Pharmaceuticals, Inc and by Takeda Pharmaceuticals America

Classification FDA classification: Locally acting chloride-channel activator
Status: prescription only

Summary

Lubiprostone is a locally acting chloride channel activator which increases gastric fluid secretion without altering sodium and potassium levels. This is the first drug of this chemical type. It is used for treatment of chronic idiopathic constipation in the adult population. Most common side effects are diarrhea and nausea, and the recommended dosage is one 24 mcg capsule taken twice daily with food.

Recommendations

The College of Pharmacy recommends prior authorization of lubiprostone with the following approval criteria"

1. Chronic Idiopathic Constipation in males and females who meet the following criteria:
    a. Have documentation that constipating therapies for other disease states have been discontinued (excluding opioid pain medications for cancer patients).
    b. Documented and updated Colon Screening. (>50 years of age)
2. Hydration and treatment attempts with a minimum of three alternate products must be documented.
3. Initial approval for 12 weeks of therapy. An additional year approval may be granted if physician documents client is responding well to treatment.
4. Quantity limit of 100 units for a 50 day supply.

Price Comparisons

	EAC	SMAC	Daily Dose*	Monthly Dose (30 day supply)
Amitiza™	$2.67	N/A	24mcg BID	$160.20
Zelnorm® 2 mg	$2.97	N/A	2 mg BID	$178.20
Zelnorm® 6 mg	$2.97	N/A	6 mg BID	$178.20
Lotronex® 0.5 mg	$7.55	N/A	0.5mg BID	$453.00
Lotronex® 1 mg	$7.55	N/A	1 mg BID	$453.00
Miralax	N/A	$.06/gm	17 gm QD	$30.60
Lactulose 10g/15 ml	N/A	$.008/ml	30 ml PO QD-BID	$14.40

Pharmacological data – Lubiprostone acts locally on the chloride channels in the abdominal lumen resulting in chloride-rich fluid secretion, and does not alter sodium and potassium. Lubiprostone acts specifically on CIC-2, a normal component of the human intestine, in a protein kinase-A independent manner. Its ability to increase fluid secretion in the intestines promotes gastric motility and the passing of gastric contents, thus relieving symptoms associated with chronic idiopathic constipation.

Therapeutic indications – Lubiprostone is indicated for chronic idiopathic constipation in the adult population.

Bioavailability/pharmacokinetics

Absorption

- Plasma concentrations are below quantification because of the low systemic availability of lubiprostone following absorption. Peak plasma levels of M3, after a single dose, occur at 1.14 hours. The Cmax was 41.9 pg/ml and the mean AUC was 59.1 pg*hr/ml. High fat meals decreased Cmax by 55%, but AUC was unchanged.

Distribution

- Lubiprostone is nearly 94% bound to human plasma proteins, shown in *in vitro* studies. Studies in rats indicated minimal distribution beyond gastrointestinal tissues.

Metabolism

- Lubiprostone is rapidly and extensively metabolized by 15-position reduction, alpha-chain beta-oxidation, and omega-chain omega-oxidation. Metabolism is not mediated by the CYP450 system, but by carbonyl reductase. M3 is a metabolite of lubiprostone expressed in both humans and animals, and is formed by the reduction of the carbonyl group at the 15-hydroxy moiety. Animal studies indicate the most likely absence of systemic absorption.

Elimination

- Lubiprostone is mainly eliminated in the urine as evidenced by radiolabeled drug. Both lubiprostone and M3 are detected in trace amounts in human feces. Lubiprostone has not been studied in hepatic- or renally-impaired patients.

Dosage forms

Oral

- Capsules, each contain 24 mcg lubiprostone

Dosage range

Recommended dosage is 24 mcg (1 capsule) twice daily orally with food

Known adverse effects/toxicities

GI-watery stools, fecal incontinence, abnormal bowel sounds, frequent bowel movements
CNS-syncope, tremor, dysgeusia, paraesthesia
General-rigors, pain, asthenia, malaise, edema
Respiratory-asthma, painful respiration, throat tightness
Skin-hyperhidrosis, urticaria, rash
Psych-nervousness
Vascular-flushing, palpitations
Metabolism and nutrition-decreased appetite
Ear and labyrinth-vertigo

Special precautions

Lubiprostone may cause nausea; administration with food may reduce these symptoms. It should not be administered in patients with severe diarrhea. Pregnancy category: C (no adequate and well-controlled studies in women); Lactation: it is unknown whether or not lubiprostone is excreted in breast milk

Contraindications

Lubiprostone is contraindicated in any patient with a known hypersensitivity to the drug or any of its excipients, or in patients with a history of mechanical GI obstruction.

Drug interactions

There is a low likelihood of drug-drug interactions as evidenced by *in vitro* human liver microsome studies. Also, no protein-binding mediated drug interactions of clinical significance are expected.

Patient monitoring guidelines

Periodic assessments to determine continued need for treatment

Patient information

- Take twice daily with food

REFERENCES

1. Amitiza™ package insert (www.amitiza.com)

New Product Summaries

Oklahoma Health Care Authority
April 2006

Drug	Manufacturer	Indications	Dosage	Adverse Effects	Contraindications	New Molecular Entity	AWP/ unit
Emsam® (selegiline) transdermal system	Manufactured for Somerset Pharmaceuticals, Inc. Distributed by Bristol-Myers Squibb Company	Treatment of major depressive disorder.	Apply to dry, intact skin of the upper torso, upper thigh or upper arm every 24 hours. Initial dose of 6 mg/24hrs, doses can be increased by 3 mg/24hrs up to maximum of 12 mg/24 hours at 2 week intervals.	Headache, diarrhea, dyspepsia, insomnia, dry mouth, pharyngitis, sinusitis, application skin reaction, rash, sexual dysfunction, vital sign changes, weight changes	Known hypersensitivity to selegiline or any component of the transdermal system; concurrent use with SSRIs, SNRIs, TCAs, bupropion, meperidine, tramadol, methadone, propoxyphene, dextromethorphan, St. Jon's wort, mirtazapine, cyclobenzaprine, oral selegiline or other MAOIs, carbamazepine, oxcarbazepine, and sympathomimetic amines; patients with pheochromocytoma, foods high in tyramine.	No	Not available
Eraxis™ (anidulafungin) for Injection	Roerig Division of Pfizer Inc.	Treatment of Candidemia and other forms of Candida infections (intra-abdominal abscess and peritonitis), esophageal candidiasis.	Candidemia: 200 mg Day 1, 100 mg daily thereafter for at least 14 days. Esophageal candidiasis: 100 mg Day 1, 50 mg daily thereafter for at least 14 days.	Rash, uticaria, flushing, pruritis, dyspnea, hypotension, diarrhea, increased liver enzymes, hypokalemia, and DVT.	Known hypersensitivity to anidulafungin, any component of Eraxis™, or other echinocandins.	Yes	Not available

APPENDIX H

Food and Drug Administration
Guide: OTC Drug Review Ingredient Report

This report contains an alphabetical listing of the ingredients considered in the OTC Drug Review that were classified and published in various *Federal Register* publications. This list includes over 2,700 ingredients (records) that provide a classification history throughout the rulemaking process. This guide describes the information presented in the report.

> Every effort has been made to ensure that this report is as complete and accurate as possible, but there may be deficiencies or errors. This report is NOT an official record recognized by the FDA and should only be used as an aid in researching the status of an OTC ingredient. Please report any discrepancies or errors so that clarifications may be made in order to provide a more accurate data base.

INGREDIENT

The ingredient names are listed in bold font at the top of the first column. The nomenclature used is in accordance with the "USAN" and "USP Dictionary of Drug Names." Ingredients with no official name are included using common names preferred by the agency. In some cases, Panels reviewed ingredients as a general class rather than as a single entity. Where this occurred, the general class is shown rather than the individual ingredient.

In some cases, the name of the ingredient has changed during the OTC drug review. The more recent (current) name is used for the ingredient categorization record in this report. The previous name has been included with reference to the current name. For example, under the ingredient "phosphate, disodium," the reader is directed to see "sodium phosphate, dibasic."

PANEL

The bottom of the first column identifies the OTC Drug Advisory Panel responsible for evaluating each ingredient.

REPORT

OTC Drug Advisory Panels issued reports for various ingredients. Some panels issued more than one report. The name of reports referencing an ingredient is listed in the second column.

CATEGORY

The third column identifies the specific pharmacologic or therapeutic class (e.g., "sunscreen" or "expectorant") for each ingredient. In many cases, an ingredient is classified in more than one category. For example, the ingredient “acetaminophen” is classified in seven drug categories.

ANPR

An Advance Notice of Proposed Rulemaking (ANPR) is a published *Federal Register* document containing the conclusions and recommendations of an OTC Advisory Review Panel. This publication was designed to stimulate discussion, evaluation, and comment on the Panel's deliberations. Panel reports were prepared independently of FDA and represent the best scientific judgment of the panel members, but do not necessarily reflect the agency's position.

The OTC drug advisory panels utilized the following classification system for each ingredient reviewed:

- Category I: conditions under which OTC ingredients are generally recognized as safe and effective and are not misbranded
- Category II: conditions under which OTC ingredients are not generally recognized as safe and effective or are misbranded
- Category III: conditions under which the available data are insufficient to permit final classification at this time as Category I or II

For categories II and III, the reason for the categorization is symbolized by S (safety) and/or E (effectiveness).

PR

A proposed rule (PR) is a published *Federal Register* document containing a tentative final monograph (TFM) or regulation for ingredients in a specific drug category. A PR is based upon an evaluation of the Panel report and the comments and data received in response to publication of the ANPR. This document represents the agency's position and proposal on the ingredients.

FR

A final rule (FR) is a published *Federal Register* document containing a final monograph (FM) or regulation for ingredients in a specific drug category. An FR is based upon an evaluation of the comments and data received in response to publication of the PR. This document represents the agency's final position on the ingredients. At this stage, the categorization system (Category I, II, and III) is no longer used. Instead, references are made to applicable sections of "Title 21 [Food and Drugs] of the Code of Federal Regulations" (CFR) or the *Federal Register*.

Information for Healthcare Professionals

Gatifloxacin
(marketed as TEQUIN)

FDA ALERT [3/2006]: On February 15, 2006, Bristol Myers Squibb (BMS) issued a Dear Healthcare Professional (DHCP) letter to U.S. physicians announcing an update to the U.S. labeling for TEQUIN (gatifloxacin) Tablets and Injection. The update includes labeling changes to strengthen the existing WARNING on hypoglycemia and hyperglycemia and adds a CONTRAINDICATION for use in diabetic patients. Serious reports of hypoglycemia and hyperglycemia continue to occur in patients both with and without a history of diabetes. These events can occur throughout the course of TEQUIN therapy. The labeling has also been updated to identify other risk factors for developing hypoglycemia and hyperglycemia, (i.e., older age, abnormal kidney function, and other blood glucose altering medications being used at the same time) while taking TEQUIN (gatifloxacin), and includes a recommendation for close medical monitoring.

FDA will review all available data and determine whether additional changes to labeling, or other regulatory actions, are warranted.

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

To report any unexpected adverse or serious events associated with the use of this drug, please contact the FDA MedWatch program using the contact information at the bottom of this sheet.

Considerations

- Tequin is contraindicated in patients with diabetes mellitus
- In addition to diabetes, other risk factors associated with dysglycemia while taking TEQUIN include older age, renal insufficiency, and concomitant glucose-altering medications (including but not limited to hypoglycemic medications, corticosteroids, diuretics). Patients with these risk factors should be closely monitored for glucose disturbances.
- **Serious reports of hypoglycemia and hyperglycemia have also occurred in patients without a history of diabetes.** If signs and symptoms of either hypoglycemia or hyperglycemia occur in any patient being treated with TEQUIN, appropriate therapy must be initiated immediately and TEQUIN should be discontinued.

Information for Healthcare Professionals

Gatifloxacin
(marketed as TEQUIN)

Data Summary
In postmarketing experience worldwide, there have been reports of disturbances in glucose homeostasis that usually occurs within 3 days of initiating TEQUIN therapy. Most of these events were reversible although some resulted in fatal outcomes.

ADDITIONAL INFORMATION: (These are now available on MedWatch site)
http://www.fda.gov/medwatch/SAFETY/2006/safety06.htm#Tequin

February 15, 2006 Letter from BMS
http://www.fda.gov/medwatch/safety/2006/tequin_DHCP.pdf

January 2006 TEQUIN Label
http://www.fda.gov/medwatch/safety/2006/tequin_PI.pdf

FDA Public Health Advisory
Sepsis and Medical Abortion Update
March 17, 2006

The Food and Drug Administration has been informed of two additional deaths following medical abortion with mifepristone (Mifeprex). The Agency received verbal notification of the deaths in the United States from the manufacturer, Danco Laboratories. At this time we are investigating all circumstances associated with these cases and are not able to confirm the causes of death. However, all providers of medical abortion and their patients need to be aware of the specific circumstances and directions for use of this drug and all risks including sepsis when considering treatment. In particular, physicians and their patients should fully discuss early potential signs and symptoms that may warrant immediate medical evaluation.

The approved Mifeprex regimen for a medical abortion through 49 days' pregnancy is:

- Day One: Mifeprex Administration: 3 tablets of 200 mg of Mifeprex orally at once
- Day Three: Misoprostol Administration: 2 tablets of 200 mcg of misoprostol orally at once.
- Day 14: Post-Treatment: the patient must return to confirm that a complete termination has occurred. If not, surgical termination is recommended to manage medical abortion treatment failures.
- The safety and effectiveness of other Mifeprex dosing regimens, including use of oral misoprostol tablets intravaginally, has not been established by the FDA.

These recommendations are consistent with warnings in the Prescribing Information and information for the patient in the Medication Guide. FDA also emphasizes that healthcare professionals and patients should be aware of the following:

- All providers of medical abortion and emergency room health care providers should investigate the possibility of sepsis in patients who are undergoing medical abortion and present with nausea, vomiting, or diarrhea and weakness with or without abdominal pain, and without fever or other signs of infection more than 24 hours after taking misoprostol. To help identify those patients with hidden infection, strong consideration should be given to obtaining a complete blood count.

- FDA recommends that physicians suspect infection in patients with this presentation and consider immediately initiating treatment with antibiotics that includes coverage of anaerobic bacteria such as *Clostridium sordellii*.

- FDA does not have sufficient information to recommend the use of prophylactic antibiotics. Reports of fatal sepsis in women undergoing medical abortion are very rare (approximately 1 in 100,000). Prophylactic antibiotic use carries its own risk of serious adverse events such as severe

or fatal allergic reactions. Also, prophylactic use of antibiotics can stimulate the growth of "superbugs," bacteria resistant to everyday antibiotics. Finally, it is not known which antibiotic and regimen (what dose and for how long) will be effective in cases such as the ones that have occurred.

As previously provided in our July 19, 2005 Public Health Advisory, updated on November 4, 2005, the Agency is aware of four previous confirmed deaths from sepsis in the United States, from September 2003 to June 2005, in women following medical abortion with mifepristone (Mifeprex) and misoprostol. All four cases of fatal infection tested positive for *Clostridium sordellii*. All four cases involved the off-label dosing regimen consisting of 200 mg of oral Mifeprex followed by 800 mcg of intra-vaginally placed misoprostol. In addition, FDA tested drug from manufacturing lots of mifepristone and misoprostol and found no contamination with *Clostridium sordellii*.

We do not know whether these new deaths were caused by sepsis or, if they were, if they were caused by infection with *Clostridium sordellii*. However, FDA, in conjunction with the Centers for Disease Control and Prevention (CDC) and the National Institute of Allergy and Infectious Diseases (NIAID), is conducting a public workshop on May 11, 2006. This scientific workshop entitled, "Emerging Clostridial Disease," at the CDC Conference Center, Atlanta, Georgia, is being conducted to discuss the scientific and medical circumstances associated with reports of morbidity and mortality associated with *C. sordellii* and *C difficile* infections. These reports include cases and clusters of *C. sordellii* toxic shock syndrome following treatment with mifepristone, *C. sordellii* sepsis associated with skin grafts, and rapidly fatal toxin-mediated cases of community-associated *C. difficile* infection. The primary goal of the workshop is to bring together scientific and public health experts to develop a draft research agenda leading to a better understanding of the virulence, pathogenesis, host factors, and non-antimicrobial risk factors contributing to those reports.

Information pertaining to Mifeprex can be found at
http://www.fda.gov/cder/drug/infopage/mifepristone/default.htm

Information pertaining to Emerging Clostridial Diseases Public Workshop can be found at
http://www.fda.gov/cder/meeting/clostridia_disease.htm

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Date created: March 17, 2006