THE UNIVERSITY OF OKLAHOMA

MEMORANDUM

TO: Drug Utilization Review Board Members

FROM: Ron Graham, D.Ph.

SUBJECT: **Packet Contents for Board Meeting – June 8, 2004**

DATE: June 1, 2004

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

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

Call to Order

Public Comment Forum

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

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

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

Action Item – Discuss and Vote on Prior Authorization / PDL for "Statins" – **See Appendix D.**

Thirty (30) Day Notice of Intent to Prior Authorize Fuzeon™ - **See Appendix E.**

Thirty (30) Day Notice of Intent to Prior Authroize / PDL "SSRI's"– **See Appendix F.**

Thirty (30) Day Notice of Intent to Prior Authorize "ARB's" – **See Appendix G.**

Review and Discuss Maintenance Medication List / Quantity Limits – **See Appendix H.**

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

Future Business

Adjournment

Drug Utilization Review Board

(DUR Board)

Meeting – June 8, 2004 @ 6:00p.m.

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

AGENDA

Discussion and Action On the following Items:

Items to be presented by Dr. Whitsett, Chairman:

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

Items to be presented by Dr. Whitsett, Chairman:

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

Items to be presented by Dr. Whitsett, Chairman:

3. **Action Item - Approval of DUR Board Meeting Minutes – See Appendix A.**
   A. May 11, 2004 DUR Minutes
   B. Memorandum of May 11, 2004

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

4. **Update on DUR/MCAU Program - See Appendix B.**
   A. Retrospective DUR Report for January / February 2004
   B. Medication Coverage Activity Audit for May 2004
   C. Help Desk Activity Audit for May 2004

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

5. **Action Item – Discuss and Vote on Prior Authorization of Provigil™ - See Appendix C.**
   A. Clinical / Economic Review
   B. COP Recommendations

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

6. **Action Item – Discuss and Vote on Prior Authorization / PDL for "Statins" – See Appendix D.**
   A. Clinical / Economic Review
   B. COP Recommendations

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

7. **Thirty (30) Day Notice of Intent to Prior Authorize Fuzeon™ – See Appendix E.**
   A. Clinical Review / Economic Impact
   B. COP Recommendations

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

8. **Thirty (30) Day Notice of Intent to Prior Authorize / PDL "SSRI's" – See Appendix F.**
   A. Clinical Review / Economic Impact
   B. COP Recommendations

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

9. **Thirty (30) Day Notice of Intent to Prior Authorize "ARB's" – See Appendix G.**
   A. Clinical Review / Economic Impact
   B. COP Recommendations

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

10. **Review and Discuss Maintenance Medication List / Quantity Limits - See Appendix H.**
    A. COP Recommendations

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

12. **Future Business**
    A. Hepatitis C Agents Review
    B. Epogen™ / Procrit™ Review
    C. Antibiotic Review
    D. Benzo/Ambien™ Follow-up Review
    E. Vote to PA Synagis™, SSRI's, ARB's, Fuzeon™
    F. Narcotics Review
    G. Xopenex Follow-up Review

13. **Adjournment**

APPENDIX A

OKLAHOMA HEALTH CARE AUTHORITY
DRUG UTILIZATION REVIEW BOARD MEETING
MINUTES of MEETING of MAY 11, 2004

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

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

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

OTHERS PRESENT:

Steve Goodson, Pfizer	Jorge Nassar, BMS	JoAnne Hargraves, Schering
Woodie Zachry, Lilly	David Montgomery, Lilly	Brad Rice, Takeda
Aleza Tomlinson, Janssen	Angela Menchaca, Amgen	Phil Woodward, OPhA
Carter McBride, BMS	Michael Hunt, D.O.	Becky Alderson, BMS
Diana Morasch, AstraZeneca	Holly Jacques, Merck	Christi Davis O'Brien, AstraZeneca
Richard Ponder, Johnson & Johnson	Loren James	Patrick Evans, BMS
Toby Thompson, Pfizer	Jonathan Klock, Glaxo	Tim Myers, Schering
Lance Stewart, Merck	Mark DeClerk, Lilly	Tracy Copeland, Forest
David Dude, BMS	Holli Hill, Sankyo	Rebecca Waldrop, Sanofi
Ricky Conley, Boehringer Ingelheim	Kay Kaut, Amylin	Margaret Lapsley, NeighborCare

PRESENT FOR PUBLIC COMMENT:

Connie Lindsay, AstraZeneca	Thomas Henebry, OU/Pfizer
Robert Calder, Merck	Jerome L. Anderson, Cardiologist

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

1A: Roll Call

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

ACTION: NONE REQUIRED.

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

2A: Acknowledgement of Speakers and Agenda Item

Dr. Whitsett acknowledged Connie Lindsay, Dr. Thomas Henebry, Dr. Robert Calder and Dr. Jerome Anderson; public comment for Agenda Item No. 9.

ACTION: NONE REQUIRED.

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

3A: April 13, 2004 DUR Minutes

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

ACTION: MOTION CARRIED.

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

4A: Medication Coverage Activity Report: April 2004

The April 2004 activity audit noted total number of petitions submitted was 15,644 including super-PA's and special circumstance PA's. Approval/denial/duplicate percentages were indicated on the reports included in the agenda packet for this meeting. Monthly reports included in agenda packet; presented by Dr. Browning.

4B: Help Desk Activity Report: April 2004

Total calls for April 2004 numbered 17,660 (75.4% pharmacies, 9.7% clients, 6.9% physicians, 8.0% other). Monthly reports included in agenda packet; presented by Dr. Browning. Dr. Swaim asked about the DME help desk and for questions concerning SoonerCare Choice PCP's Prescriber ID's provided by OHCA/EDS. It is a requirement now to have the correct PCP with the client submitted with the on-line claims processing.

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 5: **LONG TERM CARE CONSULTANT PHARMACIST PRESENTATION**

Material included in agenda packet; handouts distributed at DUR Board Meeting; presented by Drs. Phil Woodward and Margaret Lapsley. Dr. Whitsett asked who benefits from the consultant pharmacist reducing costs in the nursing home? Margaret explained that it benefited the nursing home when they have to pay for some of the medications and also her employer can show that they do help reduce costs for their customers and overall medical expenses are reduced. Safety issues can actually save money too. Dr. Whitsett asked if the Board could be comforted in knowing that most consultant pharmacists are fairly conscientious in their duties. Margaret stated that pharmacists make recommendations to physicians and then the physicians decide if they want to make appropriate changes or leave it as prescribed. Dr. Whitsett asked about the Off-Label use of antipyschotics in the nursing home population. Dr. Lapsley reminded the Board that there are no current antipsychotics available with indications for Dementia and behavioral problems in the elderly. She stated that is the number one reason they are used in the nursing home population. One problem that consultant pharmacists have is getting the proper diagnosis for these patients. Sometimes there are not any documented symptoms which are common with these types of diagnoses. Symptoms such as hallucinations and delusions may be apparent but are not documented in the charts. Dr. Whitsett asked about the safety and efficacy of these products and questions have been raised for this class of medications for those Off-Label conditions. Dr. Whitsett said there is evidence of mortality and other issues associated with these medications. Dr. Lapsley stated that this is of concern for the pharmacist also and they have started looking at other indicators such as sugar levels and diabetes and look for history of stroke and check to see what kind of antipsychotic the patient is taking. The consultant pharmacist will then make a recommendation of possibly another medication or ask the physician to consider the risks against the benefits. Dr. Whitsett asked if the pharmacist

recommends dosage reduction? Dr. Lapsley stated that every 4 months it is required by law that dosage be evaluated for antipsychotics. Patients that come into the nursing home on high doses for antipsychotics are evaluated and recommendations are given to the physician to lower it to at least the highest recommended level for the elderly that the FDA approves. Dr. Whitsett asked what the percentage of nursing home clients that is taking antipsychotics? Dr Lapsley said she thought it was around 23% nationally. Dr. Whitsett asked if there are any trends developing in nursing homes as far as medications are concerned? Dr. Lapsley said she thought that the anti-epileptics are on the increase for uses similar to the antipsychotics and the reason she stated was because of no regulations on that particular class of medications. Dr. Graham asked if she felt that there is an overuse of benzo's in the nursing home? Dr. Lapsley indicated that this region of the U.S. has a higher usage than other regions. Dr. Lapsley stated that she thought that a lot of this higher use was due to staffing shortages within the nursing facility. She thinks it is probably easier to relax a patient than to re-direct them. Dr. Lapsley said they make recommendations to the physicians to get patients off of benzo's at least every 2 months because of regulations requiring it. Routine dosing is usually recommended being changed to as needed dosing. Dr. McNeill asked how many nursing homes does her company service at this time and if calculations of savings to medicaid have been done. Dr. Lapsley said they have 25 nursing facilities currently and are in the process of calculating savings at this time. Dr. McNeill asked if there has been any resistance from the providers (PCP's)? Dr. Lapsley said that usually they don't really look at that but sometimes the physician may agree to a recommendation but the provider won't pay for it.

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 6: **REVIEW OF OKLAHOMA STATE LAW & AGENCY POLICY FOR ADDING CATEGORIES TO THE PRODUCT BASED PRIOR AUTHORIZATION PROGRAM**

Materials included in agenda packet; presented by Dr. Nesser. Dr. Hollen requested a copy of slides presented at tonight's meeting. Dr. Nesser agreed to furnish these.

ACTION: NONE REQUIRED.

AGENDA ITEM No. 7: **ANNUAL REVIEW OF ANTIHYPERTENSIVES – VOTE TO PRIOR AUTHORIZE CADUET™**

Materials included in agenda packet; presented by Dr. Moore.
Dr. Hollen wanted to know administrative costs for PBPA of antihypertensives.
Dr. Gourley moved to approve; motion seconded by Dr. Robinson.

ACTION: MOTION CARRIED.

Utilization Data for the Angiotensin II Receptor Blockers (ARB's) and Combination products was provided to the Board. Dr. Whitsett asked if there was any utilization information available on how Oklahoma Medicaid patients such as the diabetic population and heart failure population are doing with ARB's? What percentage of these clients are taking advantage of this class of drugs. Dr. Moore stated that the COP will be bringing that information to the Board in the future.

AGENDA ITEM NO. 8: **REVIEW & DISCUSS SSRI's**

Materials included in agenda packet; presented by Dr. Gorman.
Dr. Whitsett wanted to know percentage of usage for LTC facilities. Dr. Gorman said that would be looked at and brought back to the Board for review. Dr. Whitsett reminded the Board members of some of the recent emergence of adverse effects in the elderly population with this category.

ACTION: NONE REQUIRED.

AGENDA ITEM NO. 9: **THIRTY (30) DAY NOTICE OF INTENT TO PRIOR AUTHORIZE/ PREFERRED DRUG LIST HMG-CoA INHIBITORS (STATINS)**

For Public Comment; Connie Lindsay: *Connie Lindsay with Astra Zeneca. I'll see how fast I can talk. I'll be speaking about Crestor® in the treatment of dyslipidemia. I want to touch briefly about efficacy. Crestor® does offer the greatest efficacy in the statin class with a 52% reduction in LDL at below 2 mg dose. There's an added benefit with Crestor® in that you do see an actual increase in HDL at every dose. The increase is generally between 8 and 14%. This is important when you consider that a one point reduction in LDL offers a one point decrease in cardiovascular risk. A one point increase in HDL offers a 3% reduction in cardiovascular risk. There is a 1:3 ratio. Physicians are very frustrated with trying to get patients to their LDL goal and there's an attenuation with HDL that will not happen with Crestor® . I'd like to talk briefly about compliance, particularly with this patient population. Compliance is not always easy and follow-up is not always easy. Eight out of ten patients will get to goal regardless of their risk category, whether they're diabetic, CHD risk equivalent, eight out of ten patients at just below 10 mg dose. So what that means is when a patient is diagnosed, a prescription is written for Crestor®, then that patient eight out of ten times, they're going to be at goal whether they really do follow up with you as a physician. We've recently heard information out of the ACC in New Orleans that confirmed again that lower is better. Not our trials but through the trials presented as well as reversal showing and demonstrating that we probably will see updates in the incept guidelines again, telling us that 100 mg LDL is not good enough for patients that are at risk. Crestor® will meet that need with the efficacy of a 52% reduction at the 2 mg dose. At the last meeting, I know there was some questions about safety, simply because our product is fairly new. I want you to know now that we've been in the market now for, in the U.S., 9½ months. We have a million prescriptions, or a million patients, two million prescriptions. Crestor® is now approved in 52 countries. We submit, on a weekly basis, adverse events to the FDA. We're required to do that by law. The FDA does quarterly intense in-depth scrutiny of our product. They just completed the last one in March and everything looked good. Everything looked, post clinical trials compared to pre side effects, everything looked pretty much in line. There were no changes or additions to our product labeling. Also just a reminder that our landmark trial which was the Stellar Trial, was the largest comparative trial that the FDA had ever seen before a product was approved, with over 10,000 patients, and that trial demonstrated all of the efficacy data that I just told you. I also want to let you know that, let's see, I don't want to forget anything . . . There was also a recent article published in Cardiology of April by Dr. Vidt that looked at over 10,000 patients on Crestor® for an average of 3.8 years and it did demonstrate a regression in renal disease which has also been demonstrated by the other statins. So that's really about it. Do you have any questions for me?*

Dr. Hollen: *In addition to HDL do you have any information with effect on like triglycerides, lipoprotein relay, some of the other independent risk factors for heart disease?*

Ms. Lindsay: *Yes. All of those, and everything is positive. We have a good reduction on triglycerides that is similar to the other statins as well as the CRP's and little a and little b.*

Dr. Hollen: *OK. So you actually have CRP?*

Ms. Lindsay: *Yes. You can request . . . I can have that information sent to you personally or to the Board. I don't know really how that works.*

For Public Comment; Thomas Henebry: *I'm Tom Henebry, an interventional cardiologist at OU and also speaking on behalf of Pfizer. I want to talk very briefly, it's hard to be as eloquent as the previous speaker about the clinical efficaciousness of atorvastatin. I think as a cardiologist, we always look for outcome days and that's what I'm trying to present briefly. In primary prevention, the ASCOT trial, 10,000 patients, 36% reduction in days per cardiovascular events. In secondary prevention, 43% reduction in days, just days alone, number needed to treat less than 50 in the REGRESS Trial. The REGRESS trial and the MIRACLE trial combined four-and-a-half thousand patients, 50% reduction in stroke, which was a pleasant side effect. Recent study in the American Journal of Kidney Disease, diabetics on ACE and ARB for at least a year atorvastatin added a protein urea previous 2 grams reduced to 1 gram per day. Two major recent trials, our prior speaker mentioned, both changed the guidelines, I think that's one thing we all probably can agree on. Reversal trial, looking at atherosclerosis with intracardial ultrasound progression was stopped by atorvastatin, 4% progression with pravastatin. PROVE-IT trial was more important, it was funded by, not by Pfizer and is a clinical enterprise, and in that trial, atorvastatin was proven more efficacious than pravastatin, and I think we all can see the guideline going to somewhere LDL 75 to 80 mg percent. Safety data's important to those of us who remember Baycol™. We are in a similar situation before and more than 12,000 people randomized for good safety data. In the FDA pink sheet for various statins, we see the dose reduction and the incidence of 1 to 2+ protein urea. Most of the statins do what is expected and otherwise there was little need to, there was no Warfarin interaction with atorvastatin of clinical significance and no need to bother basic metabolic panels. I think to summarize I think we should from a clinical outcomes perspective we should let atorvastatin continue and view it as preferred drug.*

For Public Comment; Dr. Robert Calder: "Tape ended" . . . *Florida. Before that, I was right down the road in Ft. Sill for a couple of years as a preventive medicine officer, so, and this is my first trip back to Oklahoma in 20 years, so. I was surprised that Zocor® was not on the PDL, your proposed PDL and I'd like to offer a few comments in that regard. With respect to Zocor® 's outcomes efficacy and safety. We've heard a lot about outcomes and Zocor® has outcomes proven and in the labeling for the product. In 1994, the 4S trial, which was the first large outcome trial with a statin was published and that with over 4,000 patients, showed a 42% reduction of coronary mortality and a 30% reduction of total mortality. Following that up in 2002, we had the heart protection study with Zocor® at 40 mg which was over 20,000 patients, the largest outcomes trial ever done with a statin and that trial showed a 27% reduction in coronary events, 13% reduction in total mortality and an 18% reduction in coronary mortality. That was driven by a 38% reduction in coronary events, and not a fatal one. And so, as a result of these trials, Zocor® has outcomes in its' labeling, in our labeling, that the other statins don't have. With respect to efficacy, the 40 mg starting dose of Zocor® which is the recommended usual starting dose for Zocor® for people who are at high risk of an event, as it provides a mean LDL reduction of 41%. One study of typical CHD patients, the GOALS trial which was in patients who had CHD with LDL's of 150 to 180, 87% got to goal on Zocor® 20 to 80 mg, mean dosage 25 mg. Also Zocor® is also indicated to reduce triglycerides and to raise HDL. And it's also important when you're comparing the statins to compare the statins in the same head-to-head trial, and the same patient population because as an epidemiologist, I can tell you there's a lot of variation with all of the statins in any given patient population. The mean reduction might be 40% for example, but the 95% confidence interval on the standard deviation, not the, not the, not the standard or the mean, but the standard deviation, is plus or minus 24%, so when you're comparing two statins, even in the same patient population, the means really tell you partly they certainly are important statistically meaningful, but you have to at the patient level, remember that there's a wide range in effect. I used to say that you can drown crossing a creek with a mean depth of six inches. The mean can hide a lot of information particularly appropriate here. With respect to safety, the safety of Zocor®, there've been over a 160 million prescriptions for Zocor® written in the United States alone in the twelve years it's been on the market. And we take safety of course very seriously and like all of the statins, there have been reports of myopathy and rhabdomyalysis, rare reports with Zocor®. We don't recommend using Zocor® with potent CYP3A4 inhibitors and there are six of those listed in our labeling. We have relaxed our restrictions somewhat on . . . well we have relaxed it on niacin and fibrates other than gemfibrozil, and but again we don't recommend using more than ten of Zocor® with cyclosporine or gemfibrozil. In summary again outcomes efficacy and safety I think is what you should consider. And in addition to that, it's important to remember that Zocor® goes off patent June 23rd, 2006 and I understand that's an important factor obviously in your, in your calculations for how much money you'll save with various statins. And where you don't need a crystal ball to know whether or not Merck will fight the patent expiration because we won't. When it goes off patent June 23rd, that's it . . . it goes off patent. We extend the patents only through legitimate scientific studies and there are none of those in the offing for that. So, thank you very much and I welcome questions.*

For Public Comment; Jerome L. Anderson: *Thank you. I'm a cardiologist at Integris and Deaconess hospitals. I'm director of cardiac research at Southwest Integris and was involved in a PROVE-IT study that was mentioned earlier published here in April. So I wasn't paid to be here although I'm going to have to acknowledge Mr. Dude from Bristol Myers did alert me to the meeting. Currently I use all the statins and currently I speak for all the companies whether it's Zocor®, Pravachol®, or Lipitor®, Crestor®, and currently prescribe all those drugs and I think there's some market share information in this handout here. That probably is typical for a lot of practices in Oklahoma . . . where Lipitor® and Zocor® and Pravachol® are the big three, and Crestor® currently climbing in market share. At Baptist Hospital with the acute coronary syndrome, we're currently getting a report card, all cardiologists. You get admitted with chest pain, you're supposed to get a lipid profile and get one of these agents started in the hospital. If you don't do that, unstable angina, then you get your report card is lowered, compared to your compatriots there. At discharge, same way after bypass surgery or after a stent or after unstable angina's been diagnosed and treated, discharge on a statin is also part of your report card. It's not a, don't get fined or get physical beating, but you get compared to your colleagues, but that's part of the utilization we use at Baptist Hospital . . . drawing the lipids and treating the lipids on date of admission and discharge. So part of the argument here I think is not necessarily which statin is better as far as utilization of all the statins more often and there is the study from a recent meeting in New Orleans, one of our speakers talked about and less than 30% are on adequate Pravachol® doses or less than 40% are on adequate Zocor® doses of people admitted to the hospital, and 1% are on 80 mg of Lipitor®, so when you try to look at the PROVE-IT data and I was involved in that data at the, our local hospital, they're comparing 40 of pravastatin with 80 of the atorvastatin and, involved those patients and I think that study has some good points. It did not show reduced mortality, it did show reduced combined endpoints in hospitalization and recurrent angina where those, some of those endpoints. The mortality wasn't reduced so the endpoint data with 4S and the endpoint data with CARE and LIPID and West of Scotland, all those data points are very important. Mortality data and even the MIRACLE trial which was rehospitalization, primarily, and acute*

coronary syndromes. I think all those data are important, I don't . . . Lescol® is a drug I don't use as often as I should perhaps, and Lipitor® is not a drug I use as often as I should. I tend to use the top four products in general, and part of that reason is for certain patients Zocor® has been around a lot and a lot of my patients are still on that and stable after their heart surgery twelve years ago. Pravastatins are used in our HIV patients. I take care of Dr. Brown's HIV patients, she sends them to me and a lot of them have lipid abnormalities and pravastatin is used primarily there and the same with the transplant patients, renal and cardiac and liver transplants with their lipid . . . liver function as being a concern and so I probably use all three agents similarly to your information here and I don't think there's one study that says one drug's better than another. You know, it's a cost analysis and those of us who are doctors still have a big duty to get to goal and none of the drugs do it in a perfect manner. It's more of titrating your dose and adding other statin adjutants like niacin and fibrates and stuff like that, so it's a continuing process trying to get them to goal or raise their HDL. So I am probably asking for access to all the drugs because that's how I did in my clinical practice and I don't ask them if they're on Medicaid and I don't ask my patients if they're on Medicare, if they're private pay, it's not the way I was taught at OU by Dr. Haffner and so I treat them, all the patients the same way so I think if I have a diverse patient population, diverse set of drugs with all other indications, my preference as a practitioner would be to have all drugs available. Thanks for your time.

Dr. Gourley: *Do you have therapeutic substitution in your hospital or on the statins . . .?*

Dr. Anderson: *. . . therapeutic substitution, do you mean can you use whatever you want to? Yeah. I think they do their pricing. I have a preferred product in price but we have all the agents available for inpatients.*

Dr. Graham: *Dr. Anderson, if you were designing a preferred product list, for example, and you wanted . . . what I would ask is that you would, would you agree that you would want to not upset the marketplace any more than you have to, I mean as far as, in other words, if you have . . .*

Dr. Anderson: *Well, if any of the cardiologists go along, if primary care doctors go along, if the endocrinologists go along, I mean, if I do a third of Pravachol® and a third Zocor® and a third Lipitor® currently, and 10% Crestor® and 1% generics, I might be typical of a lot of doctors and so, whether they're Medicare or Medicaid patients, I try to treat them the same, in-patients or out-patients, so I'm not using generic Mevacor® in the hospital if they're a Medicare patient or if they're 92 years old, I'm using a brand name, so I think in answering your question, we try to use drugs to their efficacious and try to get to goal, and I'm not sure Lipitor® is better than pravastatin. There's a PROVE-ITstudy, they got to 60-something with 80 of the atorvastatin but the Alliance Study was just done at the VA, they got to 95 with atorvastatin, so you got one Lipitor® study saying they're getting to 95, you've got another one saying they're getting to 67, you've got the Prove-IT trial, they got to 95, so if you're using the same doses of drugs in two different studies done at the same time, you get different lipid levels, so I'm not sure if the VA men are different than the PROVE-IT patients. Those numbers, you have to interpret them differently. I can get to goal with any of those products.*

Dr. Whitsett: *The individuals, I think you mentioned a couple that where you would start with the pravastatin, the HIV patients, because of the number of possible interactions that's going to be out there and the transplant patients, are those the two major categories in which you would first think of pravastatin?*

Dr. Anderson: *Yeah, and again being involved in the study, I might use drugs more often if I have been involved in the PROVE-IT trial or the, just like the MERIT trial, I use more metoprolol than I use carbatolol because of being involved in the MERIT trial, and so you do have a little bit of exposure through your drug studies personally, but you know Zocor® led the field for many years and Pravachol® was second in line and so as a physician for 17 years, I have that certain habit of Zocor®, Pravachol®, Lipitor®, Crestor® because of my own personal experience, but there are certain categories where you might use each drug specifically. The 4S Trial, the Heart Protection Study, you know diabetic patients treated in a hypertension study, you might if you're going to have evidence based medicine, or if I'm going to talk to a lawyer who's my patient, I get a lot of fat diabetic lawyers, but I might put him on Zocor®, because it's evidence based, and the acute care ACS syndrome with PROVE-IT and MIRACLE, those are subgroup populations. So mortality data is important and Lipitor® doesn't have as much mortality data as Zocor® does. But they're all good products. I'm not here to talk about all of them at dinner meetings they're all good products.*

Dr. Hollen: *Do you have any insight when Pravachol®'s going to go generic?*

Dr. Anderson: *'96 also.*

Dr. Hollen: *2006?*

Dr. Anderson: *2006.*

Materials included in agenda packet; presented by Drs. Gorman and Kim. Dr. Whitsett asked about the cost difference when pravastatin is combined with aspirin such as Pravigard™. He concluded by adding aspirin that product went up significantly in price. Dr. Whitsett wanted to know what percentage of our adult population is using a statin? Dr. Hollen wanted to know why were we just looking at LDL reduction with costs associated rather than other variables. Dr. Kim explained there was some comparative data at the previous meeting and that most statins are compared across the board in this manner and the other variables haven't been studied as extensively as

LDL. LDL has been positively linked with the reduction in risks. Dr. Whitsett stated that efficacy has been demonstrated without outcome data. Dr. Whitsett said that he didn't think that the DUR Board was locking out any medication by trying to propose a rational approach to try and save money if we can with an additional secondary rebate. Dr. Hollen wants to add triglyceride levels to PA criteria.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 10: **REVIEW & DISCUSS ANTIASTHMATICS (EXCLUDING INHALED CORTICOSTEROIDS)**

Materials included in agenda packet; presented by Dr. Flannigan. NAEPP Asthma guidelines were included in packet for quick reference. Medicare (CMS) reimburses for Xopenex™ at the same rate as for albuterol due to it having "no clinical advantage over albuterol" (direct quote). Recommendation was made to bring back levalbuterol and leukotriene agents for possible PA.
ACTION: NONE REQUIRED.

AGENDA ITEM NO. 11: **FDA & DEA UPDATES**

Materials included in agenda packet; submitted by Dr. Graham. Dr. Whitsett asked if there is a policy for tablet splitting or requiring tablet splitting for clients? Dr. Nesser said there is not a stated policy in favor or against tablet splitting. Dr. Whitsett stated that he thought sometimes physicians prescribed a month's supply that they intend for the client to cut in half, and stretches it out over a two month's supply. Dr. Whitsett thinks that there could be some real savings if a policy like this didn't violate any rules or laws. Dr. Hollen asked if we could include any handouts from the previous month in the next packet?
ACTION: NONE REQUIRED.

AGENDA ITEM No. 12: **FUTURE BUSINESS**

12A: Hepatitis C Agents Review
12B: Maintenance Drug List – Quantity Limits
12C: Epogen™/Procrit™ Review
12D: Antibiotic Review
12E: Benzo/Ambien™ Follow-Up Review
12F: Vote to PA Provigil™, Synagis™ and Fuzeon™
12G: Narcotics Review
12H: ARB Follow-Up Review

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

AGENDA ITEM No. 13: **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: June 1, 2004

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

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

Subject: DUR Board Recommendations from Meeting of May 11, 2004.

Recommendation 1: Annual Review of Antihypertensives – Vote to Prior Authorize Caduet™.

Recommendation for Prior Authorization Criteria

Caduet will be placed in the Product Based Prior Authorization program as a tier-2 calcium channel blocker. Approval would require:

1. An FDA approved diagnosis from each drug category (CCB and HMG-CoA Reductase inhibitor)
2. A documented failed trial of a tier-1 CCB (diltiazem, verapamil, nicardipine, isradipine (Dynacirc CR), or nifedipine).
3. Concurrent use of an HMG-CoA reductase inhibitor.

Patients currently using both Norvasc and Lipitor will be encouraged to switch to the appropriate strength of Caduet.
MOTION CARRIED.

Date: 5/3/04

Oklahoma Health Care Authority
Attention: Drug Utilization Board (DUR)
4545 N. Lincoln Blvd.
Suite 124
Ok City, OK 73105

Re: Strattera

Dear DUR:

I would like to ask the DUR to consider Strattera (atomoxetine HCL) as a first-line therapy option for attention deficit hyperactive disorder (ADHD). The American Academy of Child and Adolescent Psychiatry (AACAP) released new guidelines on April 27, 2004 recommending Strattera as a first-line therapy option for ADHD. Strattera works differently than the stimulants, as it is a norephinephrine reuptake inhibitor. Strattera provides full-day symptom control without insomnia in most children and adolescents. There has not been any evidence of an association with dependency with Strattera. It is a non-scheduled drug without the potential "street abuse" found with stimulant medications.

Strattera offers a different, safe treatment option with a lot of potential benefits. As physicians, we need treatment options to match a patient's needs.

Thank you for your consideration.

Stanley E. Grogg, DO
SoonerCare Choice/Medicaid participant
4520 S. Birmingham Place
Tulsa, OK 74135
918-742-8160
Travelok@aol.com

SOUTHERN PLAINS MEDICAL CENTER, P.C.

2222 W. Iowa Ave. • Chickasha, Oklahoma 73018
405/224-8111 • Fax 405/222-9583

May 17, 2004

Nancy Nesser, Pharmacy Director
Oklahoma Health Care Authority
4545 North Lincoln
Oklahoma City, Ok. 73105

Dear Dr. Nesser,

It has come to my attention that the Oklahoma Health Care Authority will be updating the statin choices within the Medicaid formulary. As a family physician, I see a variety of high risk patients on multiple medications. It is my practice to choose a statin based upon LDL level as well as evidence and safety. As I am sure you are well aware, many commonly used medications are metabolized by the CYP450 3A4 system which, when used in combination, can lead to drug interactions. Because of these risks it is my hope that I will continue to have Pravastatin as a choice for my patients on multiple medications.

Sincerely,

Mitch Coppedge, M.D.

MC/dgv

David L. McElwain, M.D.
Outpatient Psychiatry
1725 E. 19th ST., Ste 202-B
Tulsa, Oklahoma 74104-5419

(918) 742-2069

June 2, 2004

Ron Graham, D.Ph.
Clinical Assistant Professor, DUR/Operations Manager
Pharmacy Management Consultants
College of Pharmacy, Department of Pharmacy: Clinical & Administrative Sciences
ORI – W4403, 1122 N.E. 13th
Oklahoma City, Oklahoma 73117

Dear Dr. Graham,

I am a psychiatrist practicing in Tulsa, Oklahoma. I have between 300 and 400 patients under my care that are recipients of Medicare/Medicaid services and as such, they are currently using the approved formulary for Medicaid in Oklahoma. I am writing to you specifically concerning the differences, I perceive, between Paxil and Paxil CR.

The new formulation of Paxil CR is much better tolerated in my patients. It has become a mainstay in my practice and I would hate to see my patients forced to receive generic Paxil or old-fashioned Paxil IR if they are on Medicaid formulary. The main difference between these preparations is in the potential for weight gain. I have approximately 300 patients in my practice who are developmentally disabled adults who were formally living at Hissom. As a group, these patients have already had a significant amount of weight gain since they have moved into the community. Much of that weight gain can be attributed to various psychotropic medications but much of it is also due to poor lifestyle constraints. In this population, in particular, I have to choose psychotropic medications that are likely to promote weight loss or, at a minimum, are least likely to promote further weight gain.

Over the past year, since Paxil CR has been available, as I have switched patients from the older forms of Paxil to the Paxil CR, I have experienced a significant tendency towards weight loss in this population. And for the most part, the Paxil CR is every bit as effective as was the previous formulations of Paxil.

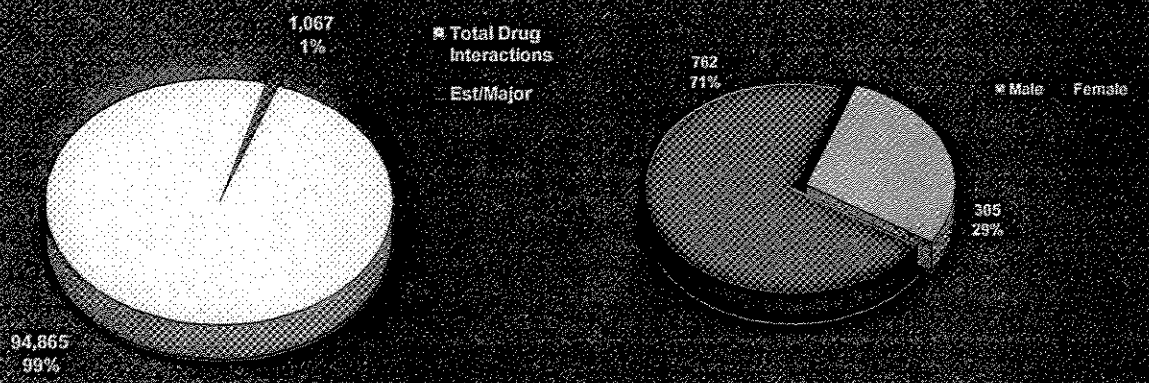
As you and your committee decide to make formulary changes for the upcoming year, I would certainly hope you would take into account the need for Paxil CR, as it has been so very important for my patients, especially the developmentally disabled patients for the reasons I have described above.

Sincerely,

David L. McElwain, M.D.
DLM/ddm

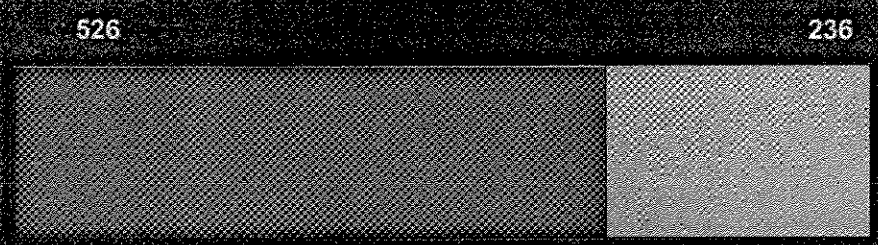
APPENDIX B

Oklahoma Medicaid RetroDUR Activity Report - Reviewed January 2004 (Female)



Oklahoma Medicaid RetroDUR Activity Report - Follow Up January 2004 (Female)

Total Reviewed = 762



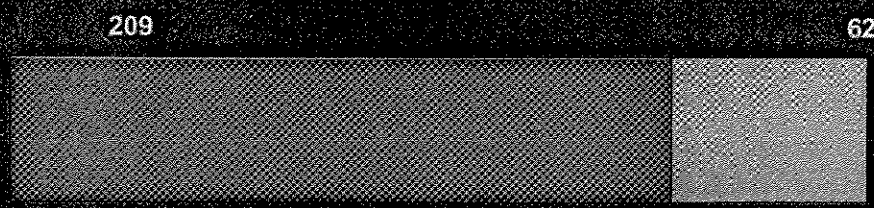
No Action Needed
Follow-Up

Total Responses		
Pharmacy =	/109	0%
Physician =	/123	0%

Oklahoma Medicaid RetroDUR Activity Report - Reviewed February 2004 (Male)

Oklahoma Medicaid RetroDUR Activity Report - Follow Up February 2004 (Male)

Total Reviewed = 271



Total Responses		
Pharmacy =	/26	0%
Physician =	/36	0%

Date Processed: Wednesday, June 02, 2004

Activity Audit for

May 01 2004 Through May 31 2004

Date	Antiulcers app.	Antiulcers den.	Anxiolytic/ Hypnotics app.	Anxiolytic/ Hypnotics den.	Antihistamine app.	Antihistamine den.	Growth Hormones app.	Growth Hormones den.	Stimulant app.	Stimulant den.	Smoking Cess. app.	Smoking Cess. den.	Nsaids app.	Nsaids den.	ACE Inhibitors app.	ACE Inhibitors den.	HTN Combos app.	HTN Combos den.	Calcium Channel Blockers app.	Calcium Channel Blockers den.	Plavix app.	Plavix den.	NPA app.	NPA den.	Misc app.	Misc den.	Daily Total
1	4	10	83	11	16	18	0	0	34	3	1	0	6	4	1	2	0	2	3	6	14	3	6	0	0	0	227
2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	4	40	185	26	28	24	3	0	46	10	0	0	13	20	3	6	1	2	2	9	26	5	9	1	0	3	466
4	19	63	248	49	51	39	0	0	71	12	0	0	24	36	0	6	2	5	4	21	42	5	12	6	3	2	720
5	15	51	193	33	45	41	0	0	76	27	0	0	12	30	3	6	2	1	1	11	24	10	18	1	3	4	607
6	9	54	188	28	35	34	0	0	70	18	0	0	9	25	2	4	4	2	7	11	31	5	16	1	1	2	556
7	11	45	195	30	53	54	1	0	72	13	1	0	6	48	4	6	1	2	4	19	36	6	18	5	1	4	635
8	5	21	54	7	8	14	0	0	15	3	0	0	6	14	1	1	1	2	3	3	7	6	17	1	0	0	189
9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
10	16	30	118	21	36	31	1	0	46	11	0	0	8	30	1	0	1	1	9	8	20	6	20	1	1	1	417
11	6	47	185	30	52	57	4	0	63	27	0	0	19	37	3	6	0	7	4	16	28	10	14	2	0	2	619
12	9	53	191	31	38	49	1	0	53	26	0	0	8	24	3	2	3	6	3	11	29	9	12	6	0	2	569
13	11	46	177	31	60	39	3	0	87	28	0	0	15	28	5	4	2	3	5	17	30	8	30	3	0	5	637
14	7	26	123	23	33	36	1	0	59	13	0	0	12	29	0	6	0	2	5	9	21	7	9	3	0	2	426
15	4	7	42	2	11	12	0	0	12	4	0	0	8	9	0	3	0	1	0	5	9	1	2	3	0	1	136
16	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
17	6	24	125	19	30	22	3	0	33	7	0	0	14	14	0	6	0	0	4	4	20	2	26	3	0	3	365
18	13	36	178	45	47	43	0	0	80	24	0	0	24	36	1	7	2	3	3	13	33	13	12	3	0	5	621
19	3	36	132	14	28	38	2	1	49	15	0	0	10	21	3	3	2	5	3	5	35	11	19	2	0	5	442
20	6	33	100	16	27	43	0	0	37	10	0	0	11	23	3	8	0	0	4	8	23	10	22	6	0	6	396
21	8	35	188	29	45	40	0	0	65	19	0	0	13	31	0	5	1	3	6	9	29	13	32	2	0	4	577
22	3	7	67	15	14	8	0	0	22	7	0	0	8	11	0	1	0	1	2	8	11	0	4	1	0	2	192
23	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
24	5	15	84	16	35	20	2	0	44	18	0	0	8	15	1	2	0	2	1	10	14	3	9	4	0	5	313
25	6	34	184	28	40	36	1	0	73	15	0	0	8	24	4	7	3	2	2	13	32	6	16	3	1	5	543
26	5	47	132	22	34	30	3	0	66	22	0	0	11	24	1	4	1	4	4	14	19	12	13	6	0	3	477
27	4	35	108	22	39	27	0	0	54	21	0	0	5	21	0	3	4	4	3	11	21	8	13	3	0	1	407
28	11	39	120	28	47	25	2	0	64	12	0	0	15	23	0	5	0	1	4	12	16	8	5	2	0	3	442
29	2	17	64	5	11	14	0	0	18	6	0	0	6	7	1	2	1	0	4	2	13	1	3	0	0	0	177
30	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Activity Audit for

May 01 2004 Through May 31 2004

Date	Antiulcers app.	Antiulcers den.	Anxiolytic/ Hypnotics app.	Anxiolytic/ Hypnotics den.	Antihistamine app.	Antihistamine den.	Growth Hormones app.	Growth Hormones den.	Stimulant app.	Stimulant den.	Smoking Cess. app.	Smoking Cess. den.	Nsaids app.	Nsaids den.	ACE Inhibitors app.	ACE Inhibitors den.	HTN Combos app.	HTN Combos den.	Calcium Channel Blockers app.	Calcium Channel Blockers den.	Plavix app.	Plavix den.	NPA app.	NPA den.	Misc app.	Misc den.	Daily Total
App.	192		3464		863		27		1309		2		279		40		31		90		583		357		10		
Den.		851		581		794		1		371		0		584		105		61		255		168		68		70	
Average Length of Approvals in Days	96		93		93		164		266		46		352		317		344		328		293		205		79		

Smoking Cessation	1 PA's for Zyban	2 Total PA's Approved
	1 PA's for Nicotine Patch	2 Unique RID's

Changes to existing PA's	794
Total (Previous Year)	8589

Monthly Totals

	Number	Percent of Total
Approved	7311	52.37%
Additional PA's	10	0.07%
SUPER PA's	724	5.19%
Emergency PA's	1	0.01%
Duplicates	759	5.44%
Incompletes	1208	8.65%
Denied *	3947	28.27%
Total	13960	100.00%

Daily Average of 558.40 for 25 Days

*** Denial Codes**

762 = Lack of clinical information	43.48%
763 = Medication not eligible	5.02%
764 = Existing PA	13.71%
772 = Not qualified for requested Tier	11.25%

SUPER PA's

Early Refill Attempts	62233
Dosing Change	473
lost/stolen/broke	81
Other	108
wrong DS	61

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

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

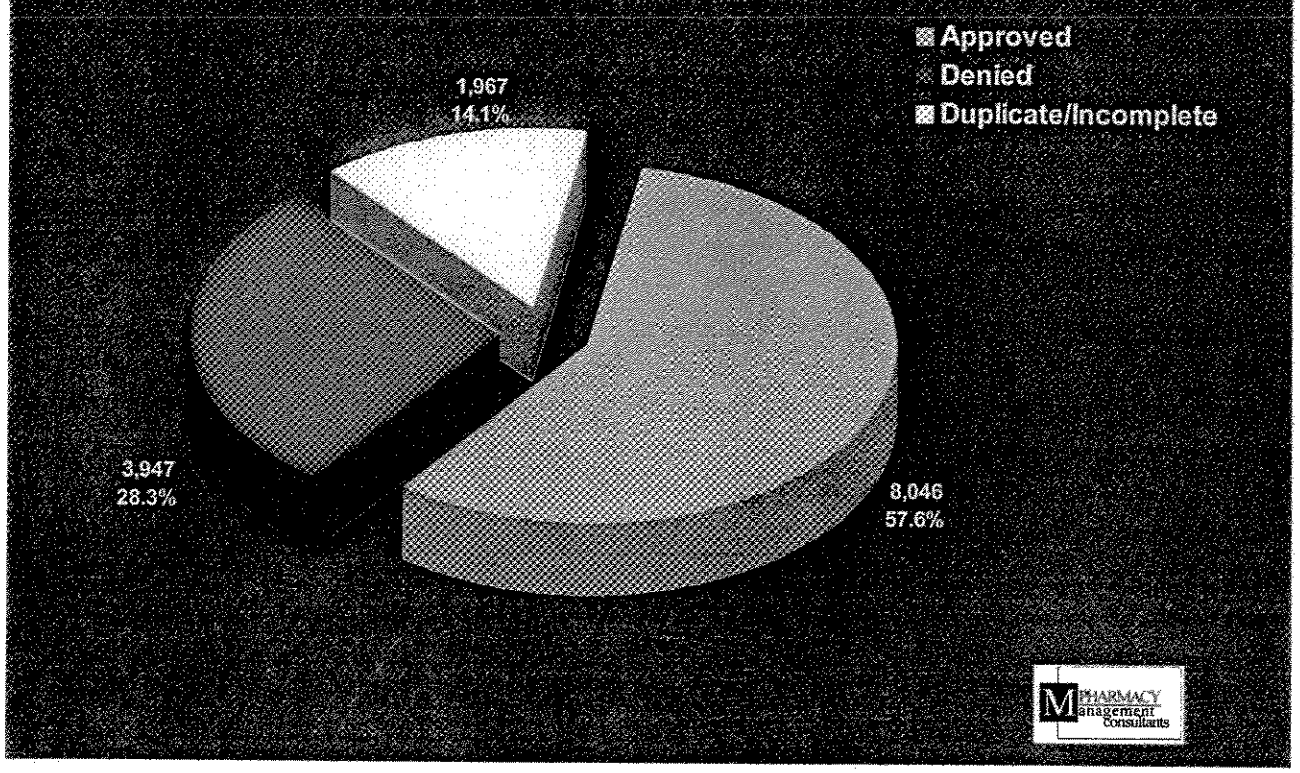
Incompletes: Missing necessary information (NDC, SIG, Diagnosis, etc.)

PRIOR AUTHORIZATION ACTIVITY AUDIT

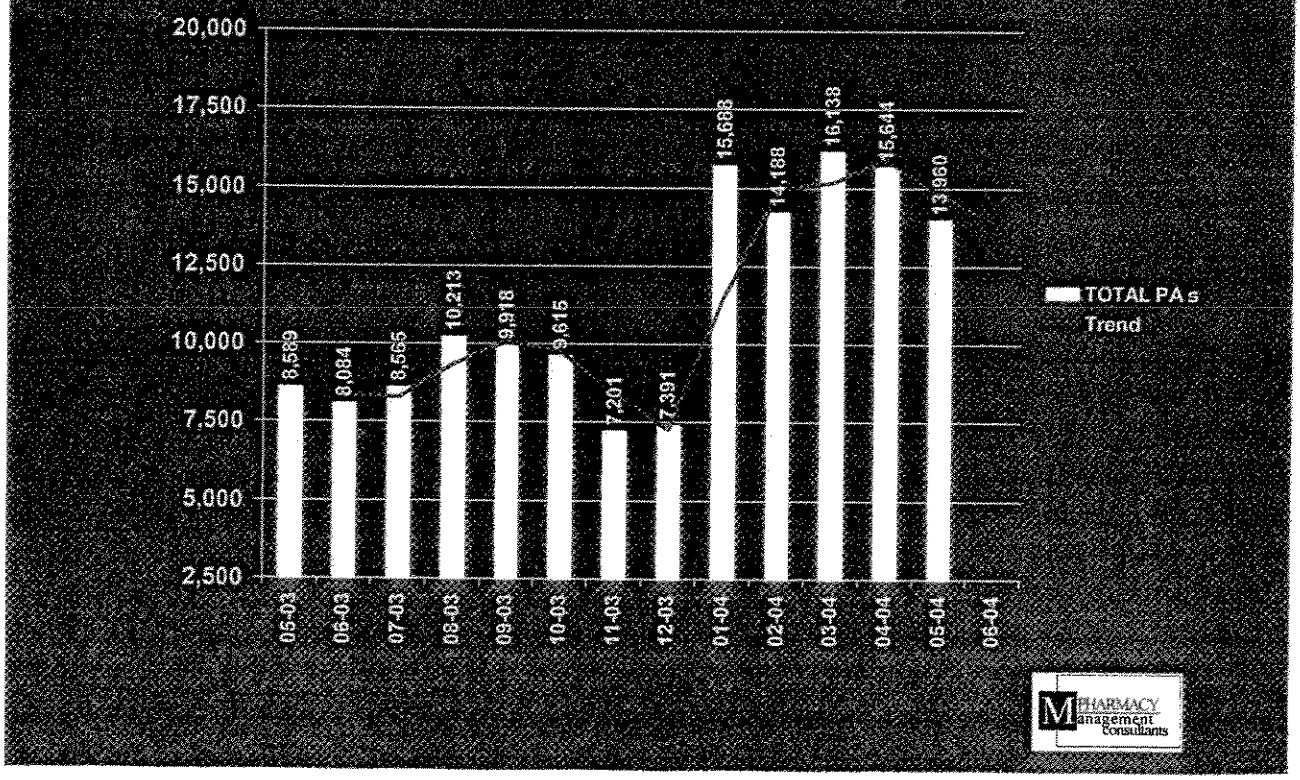
Monthly Totals

MONTH	1999 Total *(approved/ duplicates/ denied)*	2000 Total *(approved/ duplicates/ denied)*	2001 Total *(approved/ duplicates/ denied)*	2002 Total *(approved/ duplicates/ denied)*	2003 Total *(approved/ duplicates/ denied)*	2004 Total *(approved/ duplicates/ denied)*
January	4,124	8,669	9,296	8,427	7,797	15,688
February	3,542	8,077	7,194	6,095	11,272	14,188
March	3,856	7,588	7,748	6,833	10,358	16,138
April	3,867	6,390	7,676	13,381	8,953	15,644
May	3,959	6,711	7,980	12,082	8,589	13,960
June	3,884	6,565	7,249	8,550	8,084	
July	3,523	6,181	8,133	8,775	8,565	
August	10,676	7,183	8,195	9,353	10,213	
September	8,387	6,585	7,438	9,793	9,918	
October	3,863	6,140	7,956	11,584	9,615	
November	3,919	6,961	7,949	7,921	7,201	
December	3,953	6,206	6,385	4,867	7,391	
Calendar Year Total	**57,553**	**83,256**	**93,199**	**107,661**	**107,956**	**75,618**

PRIOR AUTHORIZATION ACTIVITY REPORT
May 2004

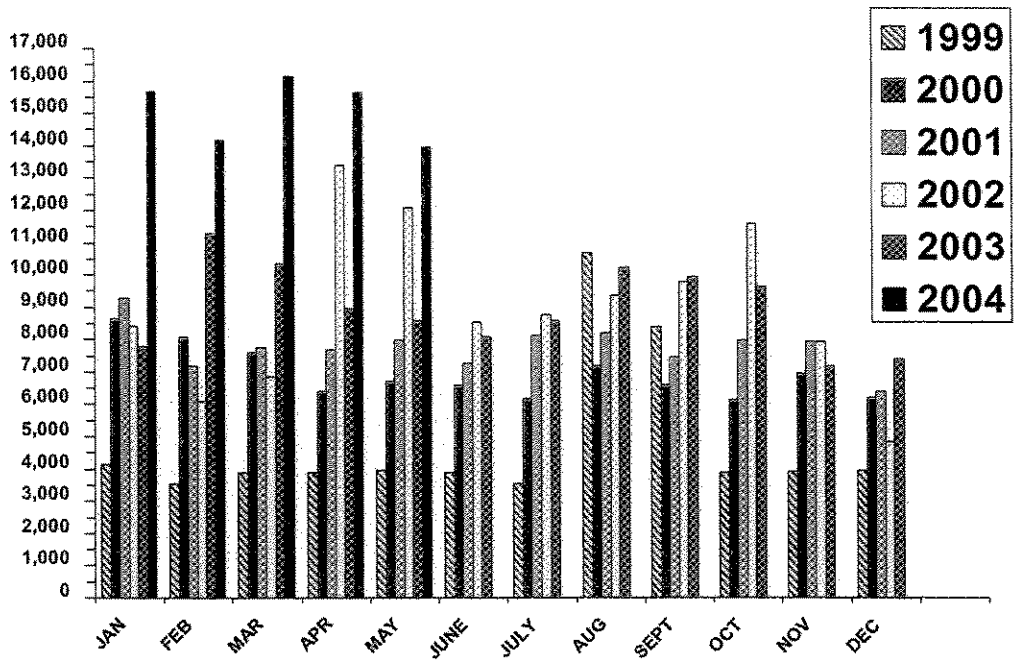


PRIOR AUTHORIZATION REPORT
May 2003 – May 2004



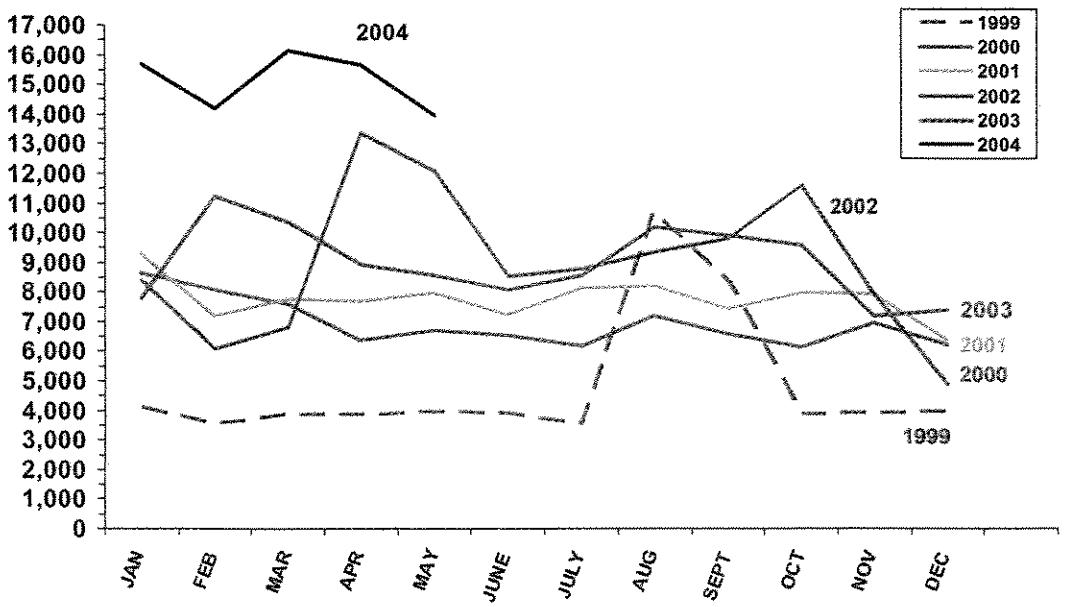
Monthly PA Activity

Calendar Years 2000-2004



Monthly PA Activity

Calendar Years 2000-2004



CALL VOLUME -MAY 2004

MAY 04	CALLER					ISSUE					TYPE OF CALL							RESOLUTION						
																				Resolved				
	Call Volume	Physician	Pharmacies	Clients	Other	Eligibility	Claims	PA Issue	SMAC	Other	Regular	Callback	Transferred Pharmacist	Transferred Supervisor	Proactive	ProDUR	Other	Helpdesk Resolved	Helpdesk PA	OHCA	Reversals/ Adjustments	EDS	Customer Service	Provider Contracts
1	295	0	260	7	28	31	227	25	0	12	264	28	0	0	0	0	3	291	1	1	2	0	0	0
2	60	0	60	0	0	16	39	1	0	4	60	0	0	0	0	0	0	60	0	0	0	0	0	0
3	906	16	797	61	32	147	530	107	1	121	805	20	1	0	1	73	6	879	4	3	16	0	4	0
4	770	17	647	68	38	125	376	107	1	161	689	29	4	0	3	41	4	758	1	4	7	0	0	0
5	719	30	603	67	19	100	393	103	1	122	673	14	4	1	3	17	7	703	1	4	5	1	5	0
6	681	13	590	48	30	95	414	62	1	109	626	12	2	0	2	31	8	666	4	2	1	0	3	0
7	625	10	574	27	14	200	287	67	0	71	604	6	0	0	1	9	5	617	0	1	5	0	2	0
8	142	0	135	5	2	85	22	29	0	6	131	0	0	0	0	9	0	142	0	0	0	0	0	0
9	47	0	38	1	6	14	22	6	0	5	38	5	0	0	0	3	1	47	0	0	0	0	0	0
10	755	16	643	67	29	109	335	172	0	139	701	8	0	4	3	24	15	736	11	2	1	0	5	0
11	731	18	631	54	28	113	341	109	0	168	696	11	0	0	2	13	9	714	13	1	0	0	3	0
12	756	17	666	37	73	101	376	159	0	120	700	19	0	0	1	23	13	733	16	2	0	1	4	0
13	780	24	658	61	37	137	325	134	0	184	688	10	0	0	5	31	22	762	15	2	0	1	0	0
14	716	14	629	57	16	94	350	103	0	169	653	8	0	0	0	41	14	702	6	0	0	0	7	1
15	193	0	179	9	5	24	113	9	0	47	179	1	0	0	0	9	4	193	0	0	0	0	0	0
16	57	0	56	1	0	8	35	1	0	13	53	0	0	0	0	4	0	57	0	0	0	0	0	0
17	745	15	665	52	13	193	391	109	0	52	695	3	3	0	0	33	11	723	13	1	0	0	3	0
18	740	22	648	43	27	142	336	121	0	141	691	18	0	0	2	25	4	736	4	0	0	0	0	0
19	642	31	513	83	15	119	228	214	0	81	588	21	0	0	3	18	12	630	5	0	2	0	5	0
20	709	31	602	60	16	358	86	209	0	56	679	11	0	0	1	9	9	700	9	0	0	0	0	0
21	716	11	602	66	37	106	352	128	0	180	657	22	0	0	5	26	6	709	0	1	0	0	6	0
22	193	0	186	5	2	32	102	19	0	40	190	2	0	0	0	1	0	193	0	0	0	0	0	0
23	57	0	53	2	2	11	35	5	0	6	54	0	0	0	0	1	1	57	0	0	0	0	0	0
24	781	17	670	76	18	101	478	121	0	80	749	8	0	0	0	20	4	766	0	2	2	0	11	0
25	781	12	701	55	13	125	466	105	0	85	753	5	0	0	0	16	7	774	0	0	0	1	6	0
26	711	10	613	74	14	113	272	237	0	89	663	11	0	0	7	17	13	703	0	1	0	1	6	0
27	724	18	613	68	25	111	417	117	0	79	667	25	0	0	3	24	5	721	0	0	1	1	1	0
28	630	28	530	56	16	129	335	88	0	78	595	11	0	0	3	12	9	615	10	0	0	0	5	0
29	166	0	122	7	0	66	100	0	0	0	166	0	0	0	0	0	0	166	0	0	0	0	0	0
30	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	**15,828**	**370**	**13,684**	**1,217**	**555**	**3,005**	**7,783**	**2,667**	**4**	**2,418**	**14,707**	**308**	**14**	**5**	**45**	**530**	**192**	**15,553**	**113**	**27**	**42**	**6**	**76**	**1**
Percentage	**100.00%**	**2.34%**	**86.45%**	**7.69%**	**3.51%**	**18.99%**	**49.17%**	**16.85%**	**0.03%**	**15.28%**	**92.92%**	**1.95%**	**0.09%**	**0.03%**	**0.28%**	**3.35%**	**1.21%**	**98.26%**	**0.71%**	**0.17%**	**0.27%**	**0.04%**	**0.48%**	**0.01%**

CALL VOLUME

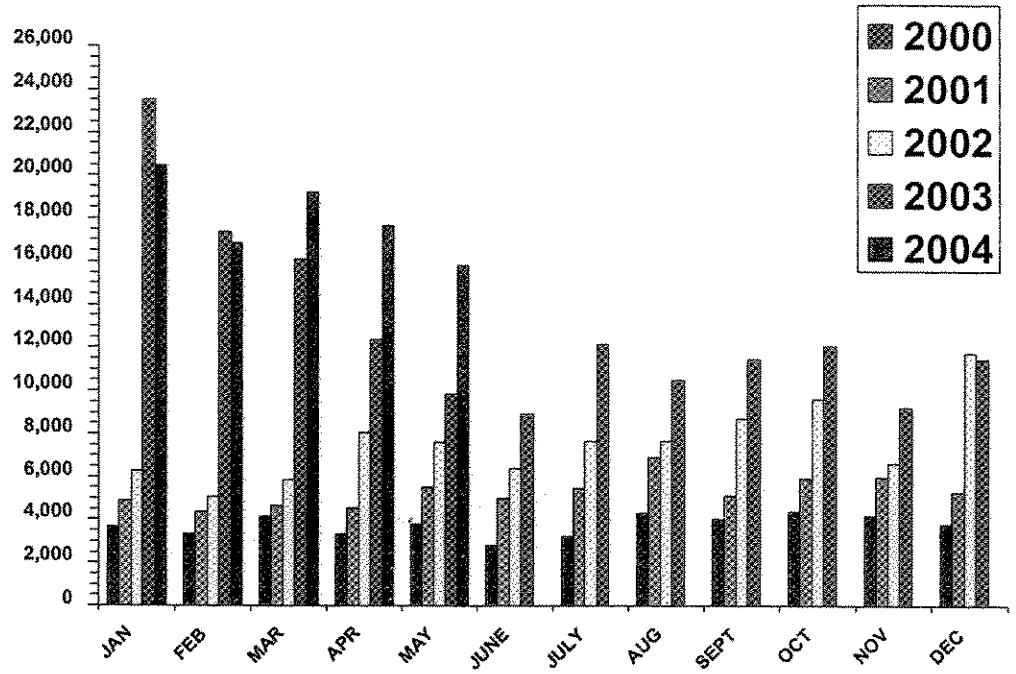
Monthly Totals

MONTH	1999 Total	2000 Total	2001 Total	2002 Total	2003 Total	2004 Total
January	* 0	3,697	4,905	6,295	23,499	20,498
February	* 0	3,335	4,393	5,049	17,354	16,857
March	* 0	4,157	4,668	5,858	16,081	19,232
April	* 0	3,337	4,556	8,047	12,378	17,660
May	* 0	3,804	5,540	7,586	9,836	15,828
June	* 0	2,820	4,982	6,368	8,917	
July	* 0	3,242	5,465	7,651	12,126	
August	3,883	4,333	6,881	7,629	10,454	
September	2,360	4,015	5,145	8,664	11,449	
October	1,963	4,398	5,912	9,608	12,102	
November	1,721	4,216	6,011	6,627	9,178	
December	2,475	3,804	5,314	11,710	11,461	
Calendar Year Total	**12,402**	**45,158**	**63,772**	**91,092**	**154,835**	**90,075**

* Help Desk Call Center implemented in August 1999.

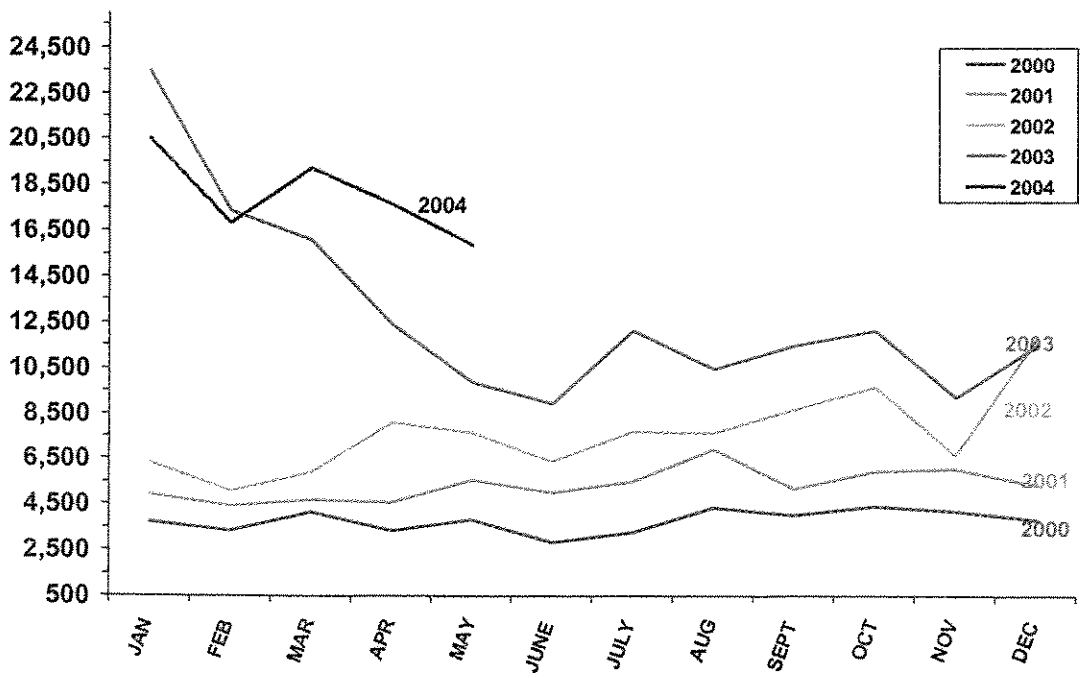
Monthly Call Volume

Calendar Years 2000-2004

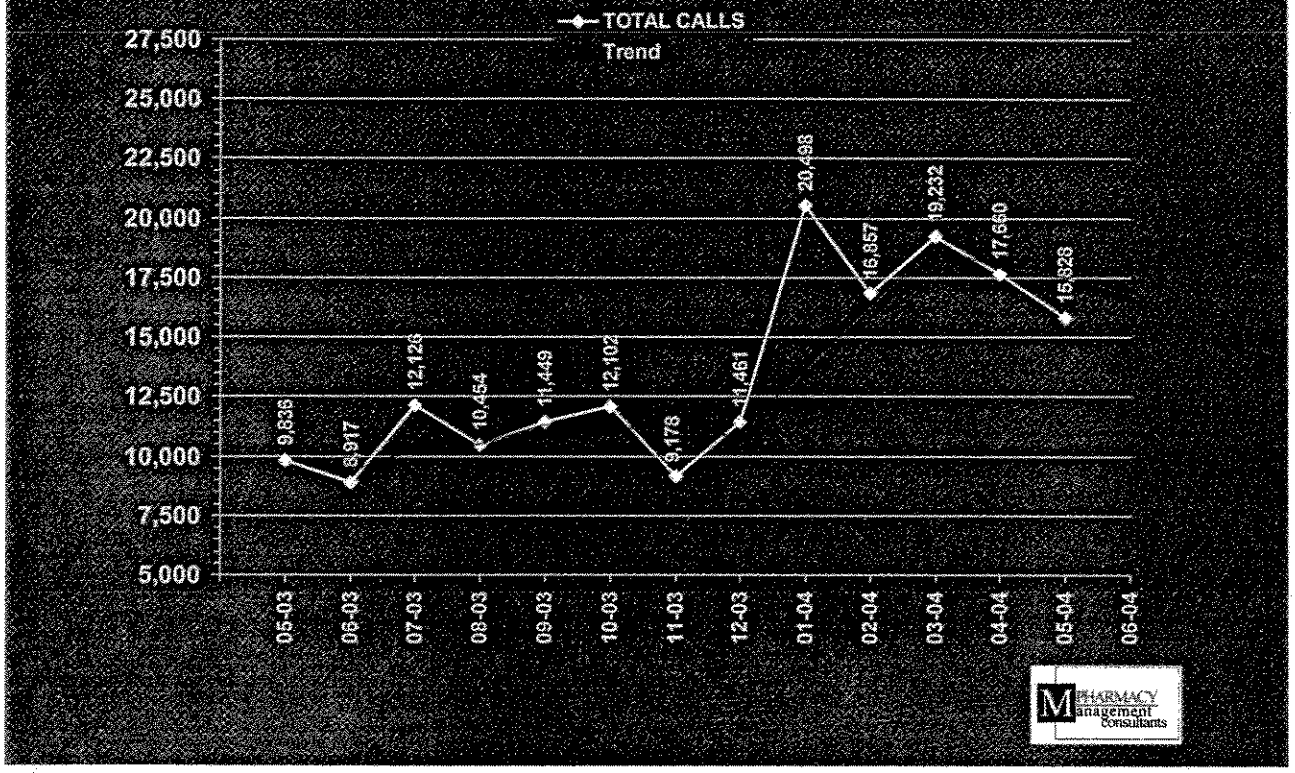


Monthly Call Volume

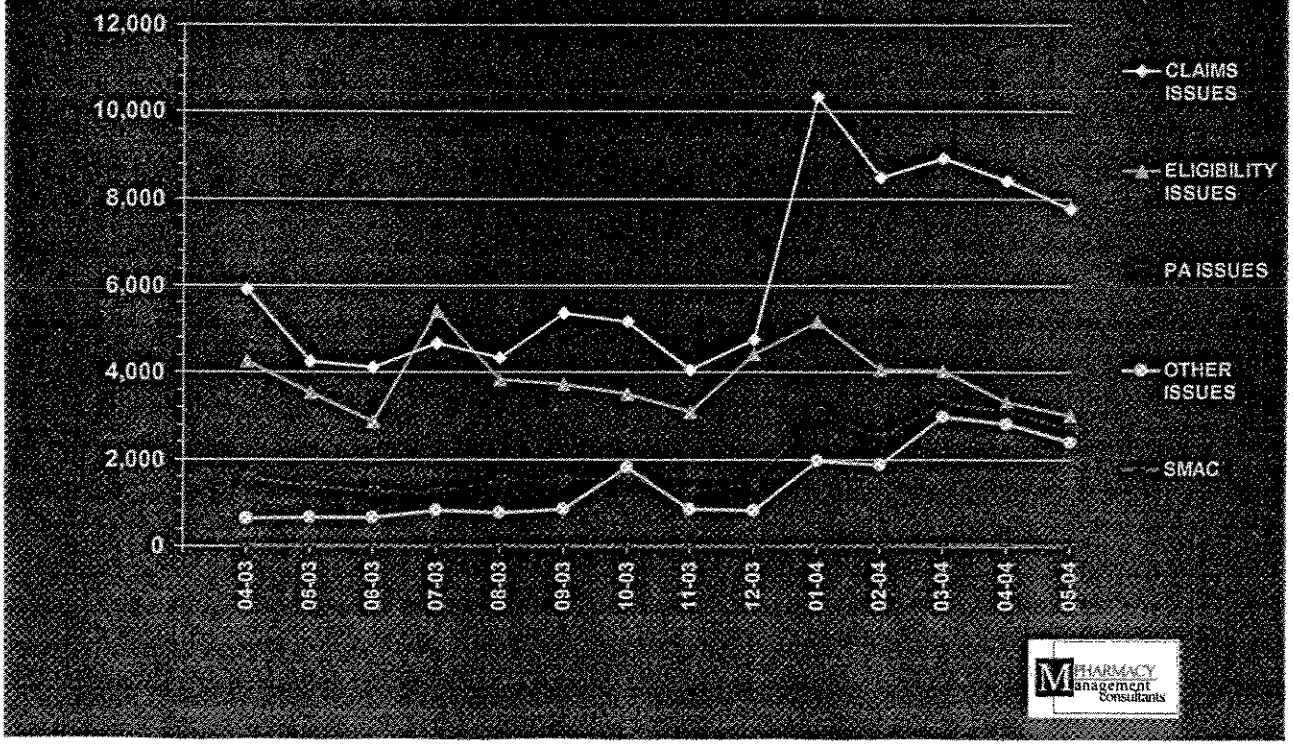
Calendar Years 2000-2004



CALL VOLUME MONTHLY REPORT
May 2003 – May 2004



CALL VOLUME ISSUES
May 2003 – May 2004



APPENDIX C

Vote to Prior Authorize Provigil® (modafinil)
Drug Utilization Review - 2003
Oklahoma Medicaid
May 2004

Drug Information

- FDA approved indications:
  - Narcolepsy
  - Obstructive sleep apnea/hypopnea syndrome
  - Shift work sleep disorder
- Off-label uses for which there are inadequate data to recommend using modafinil:
  - Depression
  - Fatigue associated with multiple sclerosis
  - Fatigue associated with fibromyalgia
  - Daytime sleepiness in patients with myotonic dystrophy
  - Alcoholic organic brain syndrome during the early phase of abstinence
  - Sleep deprivation
  - Drug-induced somnolence
  - ADHD
- Adverse reactions (a partial listing)
  - Cardiovascular: chest pain, ECG changes, hypertension, tachycardia
  - CNS: headache, dizziness, agitation, anxiety, insomnia, psychoactive and euphoric effects, alterations in mood and perception, depression, psychosis
  - GI: anorexia, diarrhea, dry mouth, hypersalivation, nausea
  - Hepatic: elevated liver enzymes
  - Ocular: dry eyes, floating bodies
- Abuse potential:
  - C IV controlled substance
  - Product package insert: "Provigil produces psychoactive and euphoric effects, alterations in mood, perception, thinking and feelings typical of other CNS stimulants…Modafinil is reinforcing….In some studies, modafinil was also partially discriminated as stimulant-like….The abuse potential of modafinil (200, 400, and 800 mg) was assessed relative to methylphenidate (45 and 90 mg) in an inpatient study in individuals experienced with drugs of abuse. Results from this clinical study demonstrated that modafinil produced psychoactive and euphoric effects and feelings consistent with other scheduled CNS stimulants (methylphenidate)."

  - Behavioural Pharmacology. 13(2):105-15, 2002 Mar. "Cocaine, but not modafinil, produced stimulant-like self-reported drug effects .... Modafinil and cocaine dose-dependently increased heart rate and blood pressure. The results of the present study suggest that modafinil has minimal abuse potential, but should be viewed cautiously because of the relatively small sample size."
  - Clinical Neuropharmacology. 23(3):149-56, 2000 May-Jun. "...modafinil has a low level of solubility in water (< 1 mg/mL) and is unstable at temperatures > or = 180 degrees C, physicochemical properties that reduce the potential for its abuse via intravenous injection and smoking, respectively. Available preclinical and clinical data on the abuse liability of modafinil suggest a much lower potential for abuse and dependency than amphetamine like stimulants commonly used for treating EDS in patients with narcolepsy."
  - Journal of Psychopharmacology. 14(1):53-60, 2000 Mar. " To compare the pharmacodynamic profiles of modafinil, methylphenidate, and placebo in humans, a double-blind Latin square crossover study was conducted in 24 male volunteers with a history of polysubstance abuse that included the stimulant cocaine.... Subjects discriminated both modafinil and methylphenidate from placebo. Subjects liked the effects of both drugs. However, modafinil differed from methylphenidate in its lack of a significant response on the Amphetamine Scale of the Addiction Research Center Inventory. The profile of physiological effects for modafinil differed from methylphenidate in that it showed greater inhibition of observed and reported sleep, less facilitation of orthostatic tachycardia and less reduction of caloric intake. These findings are consistent with preclinical pharmacological data suggesting that modafinil is not an amphetamine-like agent."
- Contraindication: Hypersensitivity to modafinil
- Precautions:
  - Cardiovascular disease
  - Hypertension
  - Elderly patients (possible dose reductions)
  - History of emotional instability, drug abuse, or psychosis
  - Severe hepatic disease (50% dose reduction)
  - Severe renal impairment
  - Patients using steroidal contraceptives (effectiveness of contraceptives reduced by modafinil)
- Pediatric and geriatric use:
  - Safety and efficacy in patients younger than 16 years have not been established
  - Safety and efficacy in patients over 65 years have not been established. Reduced doses should be considered in elderly patients

- Dosing:
  - "The recommended dose of Provigil is 200 mg given once a day…Doses up to 400 mg/day, given as a single dose, have been well tolerated, but there is no consistent evidence that this dose confers additional benefit beyond that of the 200 mg dose." (from product package insert)

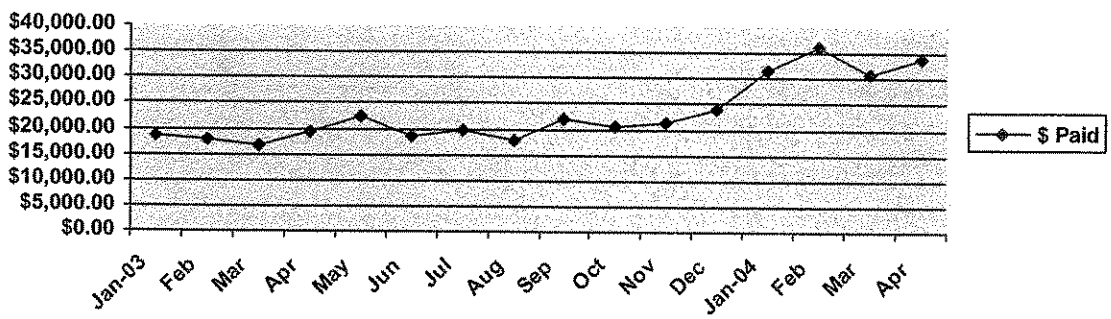
Utilization

For the period of Jan 2003 through Dec 2003, a total of 290 clients received modafinil through the Medicaid fee-for-service program.

Product	# of Claims	Total Units	Total Days	Total Cost
Provigil 100 mg tablet	278	11,846	9,651	$45,801.68
Provigil 200 mg tablet	775	36,147	28,731	$193,528.83
Total	**1,053**	**47,993**	**38,382**	**$239,330.51**

Total Cost 2003	**$239,330.51**	***= 48.6%↑***
Total Cost 2002	*$161,081.25*	
Total Claims 2003	**1,053**	***= 14.8%↑***
Total Claims 2002	*917*	
Total Clients 2003	**290**	***= 26.6%↑***
Total Clients 2002	*229*	
$ Per Unit 2003	**$4.99**	***= 12.1%↑***
$ Per Unit 2002	*$4.45*	
Per Diem 2003	**$6.53**	***= 15.4%↑***
Per Diem 2002	*$5.66*	
Mg/Day 2003	**230.6**	***= 6.8%↑***
Mg/Day 2002	*215.8*	

Provigil Cost Trend by Month, 2003 & 2004:



Claims were reviewed to determine the age and gender of the clients:

Age	Female	Male	Totals
0 to 9	6	5	11
10 to 19	9	24	33
20 to 34	35	15	50
35 to 49	61	18	79
50 to 64	33	18	51
65 to 79	29	7	36
80 to 94	19	9	28
95 and Over	2	0	2
Totals	**194**	**96**	**290**

Claims were reviewed to determine the number of claims per client:

# of Claims	# of Clients	% of Clients
1 to 5	225	77.59
6 to 10	51	17.59
11 to 15	13	4.48
16 to 20	1	0.34
21 +	0	0

Diagnostic Information from ICD-9 Coding:
Of the 290 Provigil patients, 62 had diagnoses which might indicate a disorder for which they are using the Provigil.

Diagnosis	# of Clients	% of Clients
Narcolepsy	3	1.0
Sleep Disorder	16	5.5
Multiple Sclerosis	17	5.9
Fatigue	10	3.4
ADHD	2	0.7
Depression	14	4.8

Concurrent Drug Use:

- 38 of the 290 Provigil patients (13%) used benzodiazepines concurrently with Provigil for more than 30 days.
- 28 of the 290 Provigil patients (9.7%) used opioids concurrently with Provigil for more than 30 days.
- 33 of the 290 Provigil patients (11.3%) used drugs for Parkinson's Disease.
- 16 of the 290 Provigil patients (5.5%) used drugs for Multiple Sclerosis.

Recommendations

The College of Pharmacy recommends that the board discuss this issue and consider whether prior authorization should be required for Provigil prescriptions.

Prior authorization criteria could include:

1. coverage of Provigil is limited to FDA approved indications
2. maximum approved dosing is 200 mg daily
3. quantity limitation of 30 tablets per 30 days
4. Provigil will not be approved if the patient is taking daytime benzodiazepines or other sedating medications concurrently, i.e., muscle relaxants, narcotic analgesics, other CNS depressants.
5. If the patient is using Provigil for obstructive sleep apnea/hypopnea syndrome, Provigil will be approved only if the patient is experiencing daytime sleepiness that impairs performance and quality of life in spite of the use of CPAP (Continuous Positive Airway Pressure).
6. If the patient is using Provigil for narcolepsy, trial of a tier-1 stimulant is required before Provigil will be approved. Could consider requiring sleep lab testing to confirm diagnosis, as well.
7. If the patient is using Provigil for shift work sleep disorder, specific job functions should be considered prior to approval to weigh the potential benefit of treatment versus the cost of the medication. In a study of 50 healthy young adults, modafinil 100, 200, and 400 mg was compared to caffeine 600 mg. The study's conclusion states, "modafinil does not appear to offer advantages over caffeine (which is more readily available and less expensive) for improving performance and alertness during sleep loss in otherwise normal, healthy adults."

APPENDIX D

Terminology in Dyslipidemia[1,2]

Apolipoprotein **(apo)**
- Proteins present on the surface of lipoprotein particles.
- Has a variety of functional or structural roles.

Apolipoprotein A-1 (**apo A1**)
- Structural protein of HDL cholesterol.
- Levels appear to carry little to no extra predictive power over HDL cholesterol levels.

Apolipoprotein B **(apo B)**
- Structural protein of the triglyceride rich lipoproteins and remains with the lipoproteins as it becomes TG, VLDL, IDL, and LDL.
- Also serves as the ligand for binding of LDL to LDL receptors.

Lipoprotein a – (**Lp(a)**)
- Lp(a) is a lipoprotein identical to LDL except for the addition of a highly glycosylated protein.
- Lp(a) has been associated with elevated CHD risk.
- Only niacin and estrogen show some effect in lowering Lp(a).

C-reactive protein (**CRP**)
- Marker of ongoing state of inflammation in the body.
- Recent studies show that lowering LDL also lowers CRP levels, supporting the theory that LDL itself is inflammatory and not just a cause of inflammation.

Triglycerides (**TG**)
- Esterified/oxidized free fatty acids.

Very low density lipoproteins (**VLDL**)
- Complex of TG, apo B, and various phospholipids.
- Possesses atherogenic properties.

Intermediate density lipoproteins (**IDL**)
- Hydrolyzed VLDL.
- Precursor of LDL.

Low density lipoproteins (**LDL**)
- Each LDL particle is derived from VLDL via IDL and contains one component of apo B.
- Most cholesterol found in plasma is in this form and contributes to an inflammatory process that causes atherosclerosis, plaque rupture, and thrombosis.
- Elevated LDL cholesterol is a major cause of CHD and is the primary target of therapy in the treatment of hyperlipidemia.

High density lipoproteins (**HDL**)
- Serves to transport excess cholesterol serum back to the liver.
- Low level of HDL (< 40 mg/dL) is associated with increased risk for CHD.
- Possess other protective effects such as prevention of LDL oxidation and aggregation.

Non-HDL cholesterol
- Total cholesterol – HDL cholesterol.
- Reflects the total VLDL and LDL cholesterol present in serum.

- Takes into consideration both VLDL and LDL, as both are atherogenic and account for the majority of cholesterol in serum besides HDL.
- Secondary target of therapy and highly correlates with apo B levels.

Risk Factors in Development of Coronary Heart Disease (CHD) [3]

Diagnosis of CHD includes:

1. History of myocardial infarction.
2. History of stable or unstable angina pectoris.
3. History of coronary artery procedures (angioplasty or coronary artery surgery.)
4. Evidence of ischemic heart disease by stress test.

CHD Risk equivalent:

1. Diabetes
2. Atherosclerotic peripheral vascular disease.
3. Atherosclerotic aortic aneurism.
4. Symptomatic carotid artery disease (transient cerebral attacks of carotid origin, carotid stroke, and ≥ 50% stenosis of carotid arteries.

Positive Major-Risk Factors for CHD

1. Age (male ≥ 45 years old, female ≥ 55 years old.)
2. Family history of premature CHD.
3. Current or past history of cigarette smoking.
4. Hypertension (blood pressure ≥ 140/90 mmHg, or on antihypertensive agent.)
5. Low HDL cholesterol < 40 mg/dL.

All persons with diagnosed CHD or CHD risk equivalent are considered at a high risk for developing a major coronary event. Persons without diagnosed CHD or CHD risk equivalent can use the Framingham global assessment which takes into consideration all the positive major risk factors to estimate the 10 year risk of developing a major cardiovascular event. Prevention of coronary events and/or death is the primary objective of treatment. Clinical trials have shown that LDL-lowering therapy reduces risk for CHD. Consequently LDL cholesterol is currently the primary target of cholesterol lowering therapy.

Metabolic syndrome, otherwise known as Syndrome X or Insulin Resistance Syndrome, can increase risk for CHD at any given LDL level. Management of metabolic syndrome consists of treating the underlying cause and associated non-lipid and lipid risk factors. The diagnosis of metabolic syndrome is made when 3 or more of the following are present:

1. Abdominal obesity (waist circumference exceeding 40 inches in men, 35 inches in women.)
2. Triglycerides ≥ 150 mg/dL.
3. HDL (below 40 mg/dL in men, and below 50 mg/dL in women.)
4. Blood pressure above 130/85 mmHg.
5. Fasting blood glucose ≥ 110 mg/dL.

Management of Specific Dyslipidemias:

Very High LDL Cholesterol (≥190mg/dL.)

- Primary target of therapy is to achieve LDL goal.
- Therapy often requires combined therapy of statin + bile acid sequestrant.

Elevated Serum Triglycerides

- Primary target of therapy is to achieve LDL goal.
- For high triglycerides (200-499 mg/dL) non-HDL becomes secondary target and can be achieved by intensifying statin therapy or adding nicotinic acid or a fibric acid derivative.
- For very high triglycerides (≥500 mg/dL) triglyceride lowering is the first goal to reduce risk of pancreatitis, and drug therapy should consist of nicotinic acid or a fibric acid derivative.

Low HDL

- ATP III does not specify a goal for raising HDL.
- Primary target of therapy is to achieve LDL goal.
- After LDL goal is reached emphasis should be placed on weight reduction and increased physical activity.

Diabetic Dyslipidemia

- Characterized by high triglycerides, low HDL, and small dense LDL in persons with type 2 diabetes mellitus.
- Primary target of therapy is to achieve LDL goal by statin therapy ± fibrate or nicotinic acid.

Comparison of Efficacy between Statins by Various Parameters

Statin	% LDL Reduction	% TG Reduction	% HDL Elevation	% Apo B Reduction
LOVASTATIN TAB 10MG	28	10	5	-
LOVASTATIN TAB 20MG	35	10	6.6	-
LOVASTATIN TAB 40MG	37	14	7.2	-
LOVASTATIN TAB 40MG BID	40	19	9.5	-
ALTOCOR CR® TAB 20MG	30	13	12	-
ALTOCOR CR® TAB 40MG	35	9	13	-
ALTOCOR CR® TAB 60MG	40	25	11	-
ADVICOR® TAB 500-20MG	For Titration (< 30)	-	-	-
ADVICOR® TAB 750-20MG	For Titration (< 30)	-	-	-
ADVICOR® TAB 1000-20MG*	30	32	20	-
PRAVACHOL® TAB 10MG	22	15	7	-
PRAVACHOL® TAB 20MG	32	11	2	23 (pediatric)
PRAVACHOL® TAB 40MG	34	24	12	18 (pediatric)
PRAVACHOL® TAB 80MG	37	19	3	-
LESCOL® CAP 20MG	22	12	3	19
LESCOL® CAP 40MG	25	14	4	18
LESCOL XL® TAB 80MG	35	19	7	27
ZOCOR® TAB 5MG	26	12	10	-
ZOCOR® TAB 10MG	30	15	12	-
ZOCOR® TAB 20MG	38	19	8	-
ZOCOR® TAB 40MG	41	28	13	32 (pediatric)
ZOCOR® TAB 80MG	47	33	16	-
LIPITOR® TAB 10MG	39	29	6	32
LIPITOR® TAB 20MG	43	33	9	35
LIPITOR® TAB 40MG	50	37	6	42
LIPITOR® TAB 80MG	60	45	5	50
CRESTOR® TAB 5MG	45	21	13	38
CRESTOR® TAB 10MG	52	37	14	42
CRESTOR® TAB 20MG	55	37	8	46
CRESTOR® TAB 40MG	63	43	10	54

*Due to the Niacin content of this medication the 2000/40 mg/day dose lowers Lp(a) by 22%.

Comparison of Non-HDL Cholesterol Reduction by Risk Group

Risk Category	N	% Non - HDL Reduction at 6 weeks	% Non - HDL Reduction at 54 weeks
All Patients			
Atorvastatin	1,888	33.3	38.4
Simvastatin	462	26.6	32.0
Lovastatin	472	24.1	31.8
Fluvastatin	474	17.0	25.7
Pravastatin	461	17.2	25.5
< 2 Risk Factors			
Atorvastatin	232	34.3	37.3
Simvastatin	49	27.9	31.0
Lovastatin	48	24.6	30.1
Fluvastatin	59	17.6	25.4
Pravastatin	58	18.9	23.6
≥ 2 Risk Factors			
Atorvastatin	382	33.3	36.4
Simvastatin	112	25.7	30.1
Lovastatin	95	24.1	27.7
Fluvastatin	94	16.8	24.5
Pravastatin	104	19.6	24.2
CHD			
Atorvastatin	1,274	33.1	39.2
Simvastatin	301	26.7	32.9
Lovastatin	329	24.0	33.2
Fluvastatin	321	16.9	26.1
Pravastatin	299	16.0	26.3

Adapted from Table 3 of Ballantyne CM, Andrews TC, et al. [4]

Statins and Diabetes Mellitus Type II

From 1980 to 2002, the number of Americans with diabetes more than doubled from about 5.8 million to 13.3 million. Approximately 46% of diabetics also have elevated cholesterol levels.[5] Lipid abnormalities are common in type II Diabetes and usually follow one of two patterns. The first pattern of dyslipidemia is similar to non-diabetics, characterized by primarily elevated LDL and total cholesterol. The second pattern is usually characterized by diabetes related abnormalities such as elevated TG, low HDL, and normal LDL levels.

Recently introduced is the concept that all these factors are interrelated and are all underlying causes of macro-vascular diseases. 80% of all type II diabetics eventually develop or die of macrovascular diseases (coronary artery disease, cerebrovascular disease, or peripheral vascular disease).[6] The metabolic syndrome, also called insulin resistance syndrome, or "syndrome X" is a cluster of abnormalities that includes insulin resistance, atherogenic dyslipidaemia, hypertension, obesity, and defects in coagulation, inflammation and fibrinolysis. The patients are typically centrally obese and have sedentary lifestyles. The mechanism is not yet fully understood, but it's believed that insulin plays an important role in regulation of lipid production and clearance. Insulin resistance results in increased TG and VLDL production, and at the same time reduces lipoprotein lipase activity, which reduces TG clearance. The decreased HDL is attributed to shifts of its components towards the increased synthesis of TG.[7]

LDL lowering is still the primary goal of therapy in diabetic dyslipidemia. Once LDL is at or below the desired level, the secondary target of therapy is non-HDL cholesterol. Apo B, which is present on TG, VLDL, IDL, and LDL, have been shown to be good predictors of cardiovascular risk, but is not included in the NCEP guidelines due to limited data, methodology, and availability issues. Non-HDL highly correlates with Apo B and takes into account all the atherogenic lipids. As a result, non-HDL is used as a secondary endpoint for treating diabetic dyslipidemias when LDL is not necessarily elevated.

Comparison of Diabetic Populations

Based on an inferred diagnosis using pharmacy claims for all medications classified as "antidiabetics" a total of 22,079 Medicaid fee-for-service clients can be defined as diabetic during calendar year 2003. Of the 18,490 clients receiving statins during the same time period, 6,221 clients can be defined as diabetic using the above criteria.

Percentage of Statin Claims by Drug for Client Receiving Anti-diabetic Medication

Drug	# of Claims	% of Claims
Lipitor	14,249	53.5 %
Lescol	812	3.1%
Lovastatin	372	1.4%
Mevacor	34	0.1%
Altocor	151	0.6%
Crestor	72	0.3%
Pravachol	2,458	9.2%
Pravigard	1	0.0%
Zocor	8,366	31.4%
Advicor	106	0.4%

Tablet-Splitting

Although none of the statins are scored, trials with non-scored, odd shaped tablets have shown great promise in decreasing healthcare costs without negatively affecting compliance and efficacy. Dose splitting is currently not common practice and there are many issues to consider.

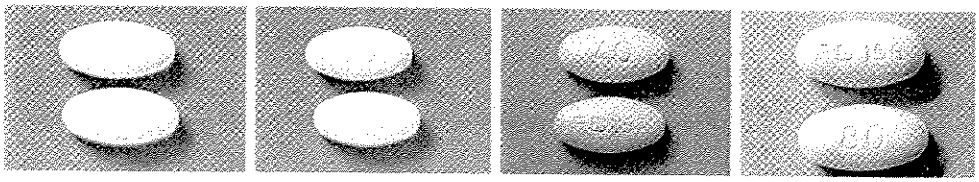
Example of Savings Using Tablet-Splitting

Previous Strength	New Example Strength	Previous Cost	New Example Cost	Potential Savings
Lipitor 10 mg	Lipitor 20 mg	$ 1,904,902.63	$ 1,374,426.90	$ 530,475.73
Zocor 20 mg	Zocor 40 mg	$ 1,940,206.38	$ 950,214.51	$ 989,991.87
Pravachol 20 mg	Pravachol 40 mg	$ 466,964.27	$ 333,172.56	$ 133,791.69
Total		**$ 4,312,073.28**	**$ 2,657,813.97**	**$ 1,654,259.29**

1. All calculations based on calendar year 2003 data.
2. No deductions were made for dispensing fees or rebates.
3. Assumes all units of previous strength would be exchanged for new example strength.
4. Assumes 1 unit of previous strength = ½ unit of new example strength.
5. New example cost = ½ previous strength units multiplied by new example strength unit cost.
6. Potential savings = previous cost – new example cost.

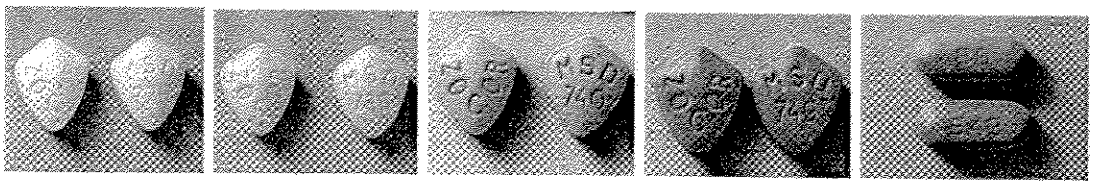
Size and Shapes of Currently Available Statins

Lipitor



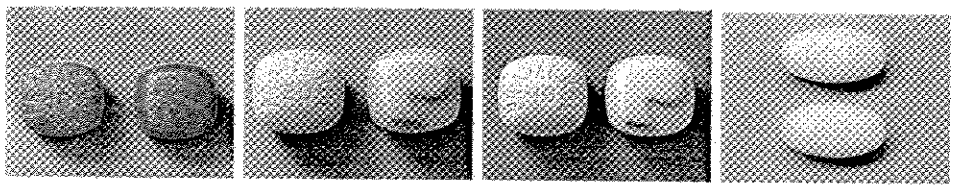
10 mg 20 mg 40 mg 80 mg

Zocor



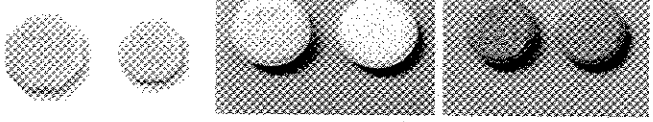
5 mg 10 mg 20 mg 40 mg 80 mg

Pravachol



10 mg 20 mg 40 mg 80 mg

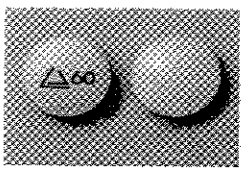
Lovastatin



Mevacor Mylan 20mg 40mg

Altocor CR

NO IMAGE
40 mg



60 mg

Crestor No Image Available.

Recommendations

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

1. Lescol and Lescol XL
2. Lovastatin (generic only)
3. Lipitor

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

1. Previous failure to achieve desired LDL or Triglyceride reduction with an initial statin - defined by at least 6 weeks of continuous therapy at standard to high dose.
2. Previous stabilization on non-preferred medication.
3. Documented increased risk for drug interactions. Specifically: concurrent immunosuppressant therapy, HIV antiretroviral therapy, and therapy with other potent inhibitors of CYP450 system.
4. Documented adverse effect or contraindication to the preferred products.

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[1] **PDR Clinical Handbook: Hyperlipidemia., 1st ed**. Copyright © 2003 Medical Economic Company, Inc.
[2] **Goldman: Cecil Textbook of Medicine, 21st ed.**, Copyright © 2000 W.B. Saunders Company.
[3] **PDR Clinical Handbook: Hyperlipidemia., 1st ed**. Copyright © 2003 Medical Economic Company, Inc.
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APPENDIX E

Fuzeon™ (enfuvirtide)
Intent to Prior Authorize

Oklahoma Medicaid
June 2004

Utilization

For the period of June 2003 through May 2004, a total of 7 clients received enfuvirtide through the Medicaid fee-for-service program. These claims were prescribed by 4 prescribers, at least 2 of whom were infectious disease specialists. All but one of the patients who were started on the drug are still filling prescriptions for it.

Product	# of Claims	Total Units	Total Days	Total Cost
Fuzeon Convenience Kit (60 single-use vials, with sterile water, syringes, & alcohol wipes = 30 days of medication per kit)	33	33	978	$60,496.81

Recommendations

The College of Pharmacy recommends that the board discuss this issue at the next DUR board meeting and consider whether prior authorization should be required for Fuzeon prescriptions.

Thirty (30) Day Notice of Intent to Prior Authorize SSRIs

Oklahoma Medicaid
June 2004

Introduction

Major depressive disorders (MDD) are the most common psychiatric disorders in the United States with a lifetime prevalence of 16.2% and a 12-month prevalence of about 6.6%.[1] In the adult population MDD is more prevalent in people who are unemployed or disabled, previously married, and of the female sex. People with chronic medical illness are at an increased risk of developing depressive disorders.[2] Nearly 75% of people who suffer from MDD also meet the criteria for at least one other psychiatric condition such as anxiety disorder, substance use disorder, and impulse control disorder. Depressive disorders and substance abuse disorders are the most prevalent disorders among adolescent suicide victims.[3] Depression can lead to physical and mental impairment which can decrease quality of life, productivity, and increase healthcare costs, especially in cases requiring hospitalization.

Diagnosis

The etiology of psychiatric illnesses such as depression is not yet fully understood. There is a 3-5 times increased risk of MDD among first degree relatives which suggests a genetic predisposition. It's also been hypothesized that repetitive episodes of illness due to significant emotional, social, or environmental stressors causes dysfunction of the normal central nervous system (CNS) processes that regulate the balance of neurotransmitters. The resultant imbalances are via alterations in neurotransmitter synthesis, breakdown, and reuptake.[4] Although there are pathophysiological changes in the CNS, currently there are no reliable physiological tests available to diagnose MDD. In the early 1950s the American Psychiatric Association compiled the first Diagnostic and Statistical Manual of Mental Disorders (DSM). Today the DSM criteria, a set of descriptive criteria, for the diagnosis of psychiatric conditions have become the standard diagnostic criteria used in clinical trials and practice guidelines for depression. The following are the diagnostic criteria for major depressive episode:

DIAGNOSTIC CRITERIA FOR MAJOR DEPRESSIVE EPISODE
At least five of the following symptoms have been present during the same 2-week period and represent a change from previous functioning; at least one of the symptoms must be A or B.
A. Depressed mood most of the day, nearly every day
B. Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day
C. Significant weight loss or weight gain when not dieting, or decrease or increase in appetite nearly every day
D. Insomnia or hypersomnia nearly every day
E. Psychomotor agitation or retardation nearly every day; observable by others
F. Fatigue or loss of energy nearly every day
G. Feelings of worthlessness or excessive or inappropriate guilt (which may be delusional) nearly every day
H. Diminished ability to think or concentrate, or indecisiveness, nearly every day
I. Recurrent thoughts of death, recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

Treatment of MDD

Treatment is primarily based upon emergent findings from clinical trials and recommendations agreed upon by consensus within the psychiatry community. There are several effective treatments for MDD such as pharmacotherapy, psychotherapy, the combination of pharmacotherapy plus psychotherapy, or electroconvulsive therapy (ECT).[5] Existing pharmacologic agents used in the treatment of depressive disorders act by influencing the level of certain neurotransmitters in the brain, mainly serotonin and norepinephrine.

The American Psychiatric Association (APA) recommends three phases in the treatment of major depressive episodes.[6] The first phase is the acute phase in which pharmacologic therapy is recommended with or without psychotherapy unless ECT is planned. This phase includes the initiation, titration, and assessment of response to therapy. The continuation phase is the 4-5 months following remission in which patients that were treated with antidepressant medications in the acute phase should be maintained on these agents at the stabilized dose to prevent relapse. The final phase in treatment is to determine, by using patient risk factors, whether to maintain the patient on pharmacologic therapy or discontinue treatment. If discontinuation is appropriate then tapering the dose is the best approach to avoid withdrawal symptoms.

The APA guidelines for treatment of depression do not recommend a specific class of antidepressant as the first line therapy in pharmacologic treatment of MDD. For decades, tricyclic anti-depressants (TCAs) were the most commonly prescribed class of antidepressants seconded by the class of monoamine oxidase inhitors (MAOIs). These agents were widely used to treat depression despite possible severe adverse effects and a great propensity for drug interactions. In 1987 Eli Lilly released the first SSRI, Prozac (fluoxetine), soon to be followed by a total of 5 more agents that now constitute the class of SSRIs. All these agents work by a similar mechanism that selectively inhibits the re-uptake of primarily serotonin, thereby increasing the level of serotonin at the synapses. Although SSRIs possess a more favorable side effect profile, efficacy and total dropout rates are similar when compared to older antidepressants.[7]

Initiation of SSRI's

- Adverse effects occur upon initiation of SSRI therapy, but effective response to treatment (if any) takes about 3-4 weeks. Hence, it's necessary to optimize tolerance of medication by letting the patient know the course of therapy and what to expect via consultation at initial visit or a leaflet sent home with the patient.
- A specific SSRI should be given at least 4 weeks of continuous use before the trial or dose is considered a failure. It is advisable to titrate up to the maximum dose of an SSRI before switching to another SSRI.
- To avoid Serotonin Syndrome do not use SSRIs within 2 weeks of MAOIs, or drugs with MAOI activity such as isoniazid and linezolid.

Adverse Effects of SSRIs

- SSRIs have similar adverse effect profiles that generally increase in severity as the dose is increased.
- The most common adverse effects are nausea, dry mouth, somnolence, headache, ejaculatory disturbances, and insomnia (occurs in > 10% of patients.)
- Other sexual side effects that occur in approximately 3-10% of patients include impotence, anorgasmia, and decreased libido.
- Hyponatremia or other electrolyte disorders may occur due to inappropriate secretion of antidiuretic hormone, especially in the elderly.

Currently Available SSRIs and Cost Comparison

Generic Name	*Brand Name*	*Dosage Forms Available*	*Dosage Range (mg/day)*	*Indications*	*2003 Market Share*	*Cost Ratio CY03[1]*	*Avg Unit SMAC FY05[2]*
Citalopram	Celexa®	10, 20, & 40 mg tabs	20 - 60	1	15.26%	2.75	
	Celexa® Solution	10 mg/10 ml			0.06%	6.45	
Escitalopram	Lexapro®	5, 10 & 20 mg tabs	10 -20	1 & 8	10.49%	2.76	
	Lexapro® Solution	5 mg/5 ml			0.02%	5.25	
Fluoxetine	Prozac®	10 mg tab; 10,20 & 40 mg cap;	20 - 80	1-3 & 7	0.40%	4.27	
	Fluoxetine	10 & 20 mg tab[3]; 10,20 & 40[3] mg cap			15.03%	1.71	$ 0.05
	Prozac® Solution	20 mg/5 ml			0.02%	2.42	
	Fluoxetine Solution				0.18%	6.28	$ 0.15
	Prozac Weekly®	90 mg delayed-release cap[4]			0.94%	3.73	
	Sarafem®	10 & 20 mg cap		5	0.05%	1.00	
Fluvoxamine	Luvox®	25, 50, & 100 mg tab	50 - 300	2	0.02%	1.45	
	Fluvoxamine				1.71%	2.43	$ 0.55
Paroxetine	Paxil®	10, 20, 30, 40 mg tab	10 - 50	1-4 & 8	17.02%	3.31	
	Paroxetine				2.89%	2.91	$ 1.73[5]
	Paxil® Suspension	10 mg/5 ml			0.09%	7.01	
	Paxil CR®	12.5, 25 & 37.5 mg tab		1, 3, 5 & 6	6.54%	3.72	
Paroxetine Mesylate	Pexeva®[6]	10, 20, 30 & 40 mg tab	40 - 60	1 - 3	N/A	N/A	
Sertraline	Zoloft®	25, 50 & 100 mg tab	50 - 200	1 - 6	29.22%	3.51	
	Zoloft® Concentrate	20 mg/ml			0.07%	2.73	

[1] Cost ratio does not reflect any actual dollar amounts.
[2] Average SMAC is based on current SMAC pricing as of 2/04 (6/04 for paroxetine) and does not include any rebates.
[3] Fluoxetine 10 & 20 mg tabs and 40 mg cap currently have a prior authorization in place.
[4] Prozac Weekly currently has a prior authorization in place.
[5] New initial SMAC pricing as of 6/04.
[6] New product as of January 2004.

1. Major depressive disorder (MDD).
2. Obsessive-compulsive disorder (OCD).
3. Panic disorder, with or without agoraphobia.
4. Posttraumatic Stress Disorder (PTSD).
5. Premenstrual Dysphoric Disorder (PMDD).
6. Social anxiety disorder (social phobia).
7. Bulimia nervosa.
8. Generalized anxiety disorder.

Recommendations

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

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

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

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

1. Documented adverse effect or contraindication to the tier-1 products.
2. Failure with a tier one medication defined as no beneficial or minimally beneficial response after at least 8 weeks of continuous use during which time the drug has been titrated up to the maximum recommended dose.
3. Current users of tier-2 products would be allowed to continue therapy without prior authorization.

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

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

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

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

References

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6 Website: **American Psychiatric Association.** Online. Internet. 2004. Available: http://www.psych.org/psych_pract/treatg/pg/Depression2e.book.cfm

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APPENDIX G

Thirty (30) Day Notice of Intent to Prior Authorize Angiotensin II Receptor Blockers (ARBs)

Oklahoma Medicaid
June 2004

Mechanism of action: The final active messenger of the renin-angiotensin pathway is angiotensin II. Angiotensin II binds to AT1 receptors to cause vasoconstriction and fluid retention, both of which lead to an increase in blood pressure. The angiotensin II receptor blockers (ARBs) lower blood pressure by blocking the AT1 receptors. Therefore they have similar effects to angiotensin converting enzyme (ACE) inhibitors, which inhibit the synthesis of angiotensin II by ACE. However, non-ACE pathways can produce some angiotensin II. ACE inhibitors also decrease bradykinin breakdown and this action could be involved in some of the beneficial and adverse effects of that class of drugs. Therefore, a potential for differential clinical effects exists for these two classes of drugs. (Therapeutics Letter, issue 28, January/February/March 1999)

Product information[1]

Angiotensin II Receptor Blockers:				
Drug	***How Supplied***	***Dosing Schedule***	***Max Dose/Day***	***FDA Approved Indication(s)***
Candesartan - **Atacand**	4, 8, 16, & 32 mg tablets	QD-BID	32 mg	Hypertension
Eprosartan - **Teveten**	400 & 800 mg tablets	QD-BID	800mg	Hypertension
Irbesartan – **Avapro**	75, 150, & 300 mg tablets	QD	300 mg	Hypertension, Diabetic II Nephropathy
Losartan - **Cozaar**	25, 50, & 100 mg tablets	QD-BID	100 mg	Hypertension, Diabetic II nephropathy
Olmesartan – **Benicar**	5, 20, & 40 mg tablets	QD	80 mg	Hypertension
Telmisartan - **Micardis**	20, 40, & 80 mg tablets	QD	80 mg	Hypertension
Valsartan – **Diovan**	40, 80, 160, & 320 mg tablets	QD-BID*	320 mg	Hypertension, Congestive Heart failure

*BID dosing for CHF

ARB Inhibitor/HCTZ Combinations:				
Drug	***How Supplied***	***Dosing Schedule***	***Max Dose/Day***	***FDA Approved Indication(s)***
Candesartan/HCTZ – **Atacand HCT**	16/12.5 & 32/12.5mg	QD	32/25 mg	Hypertension (not for initial therapy)

	tablets			
Drug	***How Supplied***	***Dosing Schedule***	***Max Dose/Day***	***FDA Approved Indication(s)***
Eprosartan/HCTZ – **Teveten HCT**	600/12.5 & 600/25 mg tablets	QD	600/25 mg	Hypertension (not for initial therapy)
Irbesartan/HCTZ – **Avalide**	150/12.5 & 300/12.5 mg tablets	QD	300/25 mg	Hypertension (not for initial therapy)
Losartan/HCTZ – **Hyzaar**	50/12.5 & 100/25 mg tablets	QD-BID	100/25 mg	Hypertension (not for initial therapy)
Olmesartan/HCTZ -**Benicar HCT**	20/12.5, 40/12.5, & 40/25 mg tablets	QD	40/25 mg	Hypertension (not for initial therapy)
Telmisartan/HCTZ – **Micardis HCT**	40/12.5 & 80/12.5 mg tablets	QD	160/25 mg	Hypertension (not for initial therapy)
Valsartan/HCTZ – **Diovan HCT**	80/12.5, 160/12.5, & 160/25 mg tablets	QD	160/25 mg	Hypertension (not for initial therapy)

1. MICROMEDEX(R) Healthcare Series Vol. 120 expires 6/2004.

Pharmacokinetic comparison[1, 2]

	Candesartan	**Eprosartan**	**Irbesartan**	**Losartan**	**Olmesartan**	**Telmisartan**	**Valsartan**
Oral Bioavailability	15%	13%	60-80%	33%	26%	42-58%	10-35%
Food Effect	no	Delayed absorption	no	10% decrease bioavailability	no	6-20% decrease in bioavailability	~50% decrease in AUC
Protein binding	99%	98%	90%	95%	99%	99.5%	94-95%
Elimination half-life (hr)	3.5-4 (parent) 3-11 (metabolite)	5-9%	11-15	2 (parent) 6-9 (metabolite)	12-18 (parent) 8-13 (metabolite)	Only 11% biotransformed	6
Active Metabolite	Yes	No	No	Yes	Yes	No	No
Metabolism	O-demethylation	Glucoronide conjugation	CYP-2C9	CYP-2C9 & 3A4	De-esterification	Conjugation	Unknown
Drug interactions	None	None	None	Rifampin, fluconazole	None	Digoxin	None
Dose in Hepatic impairment	No change	No change	No change	Reduce initial dose	No change	Use w/ caution	No change
Dose in Renal impairment	No change	No change	No change	No change	No change	No change	No change

1. MICROMEDEX(R) Healthcare Series Vol. 120 expires 6/2004.
2 Norwood, D, Branch E, Smith, B, Honewell,M. Olmesartan Medosomil for Hypertension: A Clinical Review. P&T 2002;12:611-8.

Cost Comparisons of ARBS and Tier-1 ACEIs for CY03

	Cost Ratio Compared to ARBs	CY03 Market Share	Cost Ratio Compared to Tier-1 ACEIs
Atacand®	1.85	9.46%	2.62
Teveten®	1.71	1.01%	2.42
Avapro®	1.48	17.57%	2.09
Cozaar®	1.64	32.00%	2.32
Benicar®	1.00	6.29%	1.41
Micardis®	1.10	5.36%	1.56
Diovan®	1.70	28.31%	2.40
T1 ACEI*	0.71		1.00
Atacand HCT®	1.77	4.78%	1.68
Teveten HCT®	2.76	0.35%	2.61
Avalide®	1.16	12.15%	1.10
Hyzaar®	1.40	48.40%	1.33
Benicar HCT®	1.22	0.54%	1.16
Micardis HCT®	1.00	3.69%	0.95
Diovan HCT®	1.40	30.08%	1.33
T1 ACEI-HCT*	1.05		1.00

*ACEI calculations are based on the products which were tier-1 during CY03 and do NOT include deductions for rebates.

Comments

Currently there has been no evidence to establish the ARBs as initial therapy over ACEIs or other anti-hypertensives.

Recommendations

The college of pharmacy recommends moving the ARBs into the current Anti-Hypertensive Medications Product Based Prior Authorization category.

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

1. Documented trial of a tier-1 ACE Inhibitor.
2. Documented adverse effect or contraindication to a tier-1 product.

Comparison of Sample Studies

Study	Agents	Protocol	Results
Williams, PA 2001	Olmesartan vs Captopril	Olm 5mg QD/Capt 25mg BID x 12 wks, May dbl after 4 wk & 8 wk to reponse	Sitting BP Olm -9.9 +/- 0.6 mmHg Capt -6.8 +/- 0.6 mmHg Mean BP Olm -14.7+/- 1.1mmHg Capt -7.1 +/- 1.1mmHg±
Ball, K 2001	Olmesartan vs Losartan	Olm 10mg QD/Los 50mg QD x 12 wks, May dbl after 4 wk. Could add HCTZ after 12 wks and dbl it after 16 wk if necessary	Trough seated Olm -10.6 +/- 0.5 mmHg Losartan -8.5 +/- 0.6 mmHg Mean BP Olm -14.9+/- 1.0mmHg Los -11.6 +/- 1.0 mmHg
Oprail et al 2001	Olmesartan vs Losartan vs Valsartan vs Irbesartan	Olm 20 mg QD, Los 50 mg QD, Val 80 mg QD, or Irb 150 mg QD x 8 wks	Seated Olm -11mmHg Los -8.2 mmHg Val -7.9 mmHg Irb -9.9 mmHg
CLAIM Bakris et al. 2001	Candesartan vs Losartan	Cand 16 mg QD or Los 50 mg QD, forced titration (dbl'd) after 2 wks x 6 wks	Trough Cand -13.3/10/.9 mmHg decrease Los -9.8/8.7 mmHg decrease Peak Cand -15.2 to 11.6 mmHg Los -12.6 to 10.1 mmHg
ELITE II (CHF) Pitt et al. 2001	Losartan vs Captopril	Los 50 mg QD or Capt 150 mg/d	No diff in all-cause mortality, sudden death or resuscitation arrests, but discontinuation lower with losartan than captopril
ValHeFT (CHF) Cohn et al. 2001	Valsartan plus standard tx	Standard tx = ACEI, Digoxin, Diuretic, beta-Blockers	Val - 13.2% reduction in combined end point mortality/morbidity (Card arrest w/ resuscitation, hosp for CHF, or inotrope or vasodilator tx)
ELITE (CHF) Pitt et al. 1997	Losartan vs Captopril	Los 50 mg QD or Capt 50 mg tid x 48 wks	Losartan - lower mortality. No diff in increased serum creatinine levels or hospitalization for CHF, but fewer hospitalizations for any reason with losartan. And losartan better tolerated with less discontinuation
VALIANT Pfeffer et al 2003	Valsartan vs Captopril vs combination	Capt 50 mg tid, Val 160 mg bid, or capt 50 mg tid + Val 80 mg bid	No difference in overall mortality. Pts on Captopril alone or in comb had more discontinuation

Response to Board Question regarding utilization of these classes of drugs by CHF and DM clients
Oklahoma Medicaid
June, 2004

Oklahoma Medicaid Utilization - July 1, 2002 to June 30, 2003

Drug	Total Clients	Diabetes (%)	CHF (%)
ACE-I	22,691	6,070 (26.8%)	4,679 (20.6%)
ACE/HCT	2,353	446 (18.9%)	218 (9.3%)
ARB	5,226	1,276 (24.4%)	1,002 (19.2%)
ARB/HCT	2,953	573 (19.4%)	350 (11.9%)
ACE/CCB	1,452	301 (20.7%)	174 (12%)
Totals (Unduplicated)	31,607	8,009 (25.3%)	5,981 (18.9%)

Using diabetic medication claims, it can be inferred that there are approximately 22,143 diabetic clients in the Oklahoma Medicaid population. Of these, 8,009 (36.2%) are on an ACEI, ARB, or combination drug. Using hospital claims information, it can be inferred that there are at least 14,103 clients being treated for CHF. Of these, 5,981 (42.4%) are on an ACEI, ARB, or combination drug.

APPENDIX H

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

Anticoagulation:
- cilostazol
- clopidogrel
- pentoxifylline
- ticlopidine
- warfarin

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

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

Hormone:
- conjugated estrogens
- estradiol
- estropipate
- medroxyprogesterone acetate
- tamoxifen

Cardiovascular (includes combinations where appropriate):
- acebutolol
- amiloride
- amiodarone
- amlodipine
- atenolol
- atorvastatin
- benazepril
- betaxolol
- bisoprolol
- bumetanide
- candesartan
- captopril
- carvedilol
- chlorothiazide
- chlorthalidone
- clonidine
- diltiazem
- digoxin
- disopyramide
- doxazosin
- enalapril
- eprosartan
- ethacrynic acid
- felodipine
- flecainide
- fluvastatin
- fosinopril
- furosemide
- guanadrel
- guanethidine

- guanfacine
- hydralazine
- hydrochlorothiazide
- indapamide
- irbesartan
- isosorbide mononitrate
- isosorbide dinitrate
- isradipine
- labetalol
- lisinopril
- losartan
- lovastatin
- methyldopa
- metolazone
- metoprolol
- mexiletine
- minoxidil
- moexipril
- moricizine
- nadolol
- nicardipine
- nifedipine
- nisoldipine
- nitroglycerin (all oral forms)
- olmesartan
- perindopril
- pravastatin
- prazosin
- procainamide
- propranolol
- quinapril
- quinidine
- ramipril
- reserpine
- rosuvastatin
- simvastatin
- sotalol
- spironolactone
- telmisartan
- terazosin
- timolol
- torsemide
- triamterene
- trandolapril
- valsartan
- verapamil

Thyroid:

- levothyroxine
- liotrix
- liothyronine
- methimazole
- propylthiouracil
- thyroid

Other:

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

APPENDIX I

Last Saturday, the Oklahoma Health Care Authority's Chief Executive Officer Mike Fogarty was honored with the Distinguished Public Service Award from the OSU College of Osteopathic Medicine.

Fogarty, who was invited to deliver the 2004 Commencement address to the graduates of the OSU College of Osteopathic Medicine, was completely unaware of this development until he saw it mentioned in the Commencement program. "I noticed my picture and assumed it was there because I was the commencement speaker, but the title to the page which read 'Distinguished Public Service Award' slightly puzzled me," said Fogarty.

The mystery unfolded immediately following the commencement address, which Fogarty delivered with his customary poise and inspiration. Dr. John Fernandes, President of the Center for Health Sciences and Dean of the College of Osteopathic Medicine presented Fogarty with this prestigious award that is bestowed upon individuals for achievements in the following areas:

- Development of medical education so as to embody the highest standards of excellence and dedicated teaching;
- Improvements in health care for the community, state, and nation;
- Advancement of ideals that contribute to building a better society.

The Award and the Commencement program are on display this week in the Fishbowl.

Oklahoma State University

College of Osteopathic Medicine

Distinguished Public Service Award

2004 Recipient

Mike Fogarty, M.S.W., J.D.,
Chief Executive Officer,
Oklahoma Health Care Authority

Mike Fogarty, M.S.W., J.D., is the Chief Executive Officer of the Oklahoma Health Care Authority (OHCA). The agency administers the Oklahoma Medicaid and State Child Health Insurance Programs with an annual budget of $2.6 billion.

Joining OHCA in 1995 as State Medicaid Director and Chief Operating Officer, his public service career began in 1971 as a social worker for the Oklahoma Department of Human Services (ODHS). Mike left state government in 1979 to join the legislative staff of the newly elected U.S. Senator David Boren. While on Senator Boren's Washington, D.C. staff, he had responsibility for U.S. Senate Finance Committee matters including Medicaid, Medicare, and other social and medical programs authorized by the Social Security Act.

Upon his return to Oklahoma, Mike rejoined ODHS as the agency's Deputy Director and also served as the Assistant Director for Medical Services.

For eight years, beginning in 1987, Mike practiced law and operated long-term health care facilities in Oklahoma. During this time, he remained involved in public service through volunteer community activities, including an elected term on the Oklahoma City Public Schools' Board of Education.

Under his leadership, the OHCA has expanded medical coverage for children, pregnant women, disabled and elderly adults. Oklahoma's SoonerCare demonstration project has placed a greater emphasis on prevention and early intervention, established a "medical home" for all beneficiaries, associating them with primary care physicians, physician assistants, or advanced practice nurses statewide.

Oklahoma is one of eight grantees receiving a federal grant for the purpose of development of plans that offer affordable health insurance to uninsured citizens.

Mike earned a bachelor's degree from Oklahoma Baptist University, a Master of Social Work from the University of Oklahoma, and a Juris Doctorate from Oklahoma City University. He and his wife, Billie, reside in Oklahoma City.

http://www.osu-med.com/commencement2004/publicserviceaward.htm

This Week In Medicine

Over the counter statins: Good news, but patients need to be educated

May 21, 2004

By Doug Kaufman

ST. LOUIS (MD Consult) - While the news that England will become the first country in the world to make statins available over the counter does cause some concern about patients self-diagnosing their problems, there are also several positive aspects.

The bottom line is "statins have compensated for the environment that we're in," said cardiologist Dr. Alfred A. Bove, professor of medicine emeritus at Temple University School of Medicine and editor-in-chief of Cardiosource. "... It does get the results. We're seeing substantial lowering of lipids and substantial reductions in cardiovascular risk across a broad spectrum."

In England, a low dose of the statin Zocor is scheduled to be available OTC in July. It will be sold to people deemed at moderate risk of heart disease, including men over age 55 plus men over 45 and women over 55 who smoke, are overweight or have a family history of heart disease. The move is expected in the United States eventually, but there is no specific date on the FDA timetable.

"I think the FDA is going to do it," Dr. Bove said. "We should know by the end of the year."

Dr. Bove (pronounced Bo-VAY) said there are two ways to look at the issue of OTC statins.

"A lot of patients will see a physician who will say, 'You need X, Y and Z drugs.' If they have a drug plan, it's probably cheaper to get the prescription drug," he said. "If they don't have a drug plan, they're a lot better off buying it over the counter. So, I think the first place it would be useful would be with people who don't have drug plans where their doc takes care of them and says, 'Look, you need a statin drug. Go buy this one over the counter.' I do that often. I'll write the name of a drug on a prescription form — not as a prescription but just to give the patient the name.

"They're all using over-the-counter stomach medicines and antihistamines," he said. "From that standpoint, I don't think it would be such a bad deal because it'll open up access to these medications to a large number of people."

Mevacor, for instance, is projected to sell for half the cost OTC compared to prescription, he said.

"For those patients who have to pay out of their pocket, I think it would be helpful to them," he said.

This doesn't augur the end of the doctor-patient consultation.

"I don't get the sense that most people will go measure their cholesterol with a finger stick and then go buy a statin," Dr. Bove said. "I may be wrong, but most people would still want to get some sort of (medical) advice."

While some people will self-treat, he said, making statins cheaper and more easily accessible is basically a good thing.

The typical diet in the United States, heavy on fast foods and low on fruits, vegetables and other healthy choices, is "conducive to bringing cholesterol (levels) where they are — elevated," Dr. Bove said. "Some people who have looked at various populations find that a cholesterol level of 140 with an LDL of ... 50 is probably more in keeping with what human beings had 5,000 years ago when they didn't have all this food to eat, all these rich, sweet things."

Some kind of a change needs to be made.

"Right now, I think there is a (high cholesterol) epidemic, and part of it is we can't get out from under the

foods that we eat," he said. "A lot of people say they're going to eat their steak, and have their statin. Or put the statin in the water supply. Because we can't get the food out of our environment. That's the biggest problem. ... We can't eat the diet that would get the levels of cholesterol that would truly prevent atherosclerosis."

64

The goal of maintaining an LDL level around 70 or better is difficult in a society crammed with food options and availability.

"I go through this every week with probably a half dozen patients. 'Look, change your diet. Cut down on all the fatty foods, cut down on carbohydrates, eat more green, leafy vegetables. Less meat and more fish.' So you go through that litany, and then three months later the patient comes back and nothing has changed," Dr. Bove said. "They've tried the diet but they just can't adhere to the diet because of the social pressures and the family pressures. You know, to go out and eat a strange diet when everybody else is eating something else.

"So what are you left with? 'OK, you had your three-month trial. It was unsuccessful. I don't like your lipid numbers. We've got to do something to protect you. So here comes the statin.'"

Statins have worked for a broad range of people, from those with no history of cardiac disease to those with heart disease in the family and people who have had heart attacks, Dr. Bove said.

"Everybody seems to get a benefit from taking a statin," he said. "... We're seeing a substantial number of patients benefitting from getting their lipids in line. We're now talking about cholesterols of 150, 160 and LDLs of 70 to 75. This is a proven trial, that was just recently presented. I think everybody is using as a goal, not what's recommended, but actually below that. Because we're starting to see data saying that you have to go down pretty far to protect people."

Dr. Bove has "mixed feelings" about making statins available OTC.

"We know we can protect people," he said. "I have patients, and everybody else does too, with bad coronary disease that couldn't be operated on. We put them on statins and aggressively managed their lipids, I mean really aggressively managed their lipids. And they get better, without surgery, without angioplasty. So we know it works. And the trials are beginning to support that kind of approach.

"The question is, 'What do you do?' The stuff is good," he said. "Nobody's going to die anymore, unless you get run over by a truck or something like that. These are actually preventing atherosclerotic progression and death. To me the dilemma is not to take advantage of the fact that these things work and start overcharging. This is one solution to it, to make them ubiquitous."

As good as statins are, they are not a panacea.

"They will not solve the problem of somebody who's obese, diabetic and smoking," Dr. Bove said. "It won't solve that person's problem, whether you take them 'till the cows come home. You've got too many other factors that are overriding the effects of the statin. There's still going to have to be an effort to educate the public about lifestyle modifications in addition. But given that you can get lifestyle modifications down to something that's reasonable, ... you just can't get (some) patients further down without using a statin drug."

One of the concerns about statins involves interactions with other drugs. If the wrong antibiotic is added to a regimen already including a statin, it can lead to myopathy.

Some people use niacin to lower cholesterol, but statins are better, Dr. Bove said.

"The statin drugs are easy to take, they don't have a lot of side effects, and they also have this other protective thing about protecting the endothelium or being an anti-inflammatory, which is not true of the niacins, for example," he said.

One of the concerns about statins involves interactions with other drugs. If the wrong antibiotic is added to a regimen already including a statin, it can lead to myopathy.

"You talk to (the patient) and you find out that a doc somewhere prescribed an antibiotic that blocks the

metabolism of the statin," he said. "And I'm sure, when you buy these things (OTC), there are going to be a ton of cautions on the side about what drugs you can take and what drugs you can't take (in combination). But it's very common for one physician to order a statin and another doc somewhere to order something else that will cause the level of statins to go up in the blood and cause actual muscle injury. This is one of the things I worry about, because that's not an obvious relationship. Patients are not supposed to know all the possible drug interactions."

65

Dr. Bove would like to see "patient empowerment," where patients are educated about the medicines they are taking, how they affect the body and how they interact with each other. Doctors should be proactive before prescribing.

"It's appropriate," he said, "to ask the patient, 'What are you taking?'"

Related Information

Journal Articles

Lowering LDL cholesterol reduces risk of ischaemic heart disease events
Rosenson RS - *Evidence-based Healthcare.* - March 2004; 8(1); 48-49
Full Text

Atorvastatin and rosuvastatin reduce LDL-C more than other statins
Wierzbicki AS - *Evidence-based Cardiovascular Medicine.* - December 2003; 7(4); 181-182
Full Text

What do the statins tell us?
LaRosa JC - *Am Heart J* - 01-DEC-2002; 144(6 Suppl): S21-6
From NIH/NLM MEDLINE
Review Full Text Abstract

Efficacy and safety of ezetimibe added to ongoing statin therapy for treatment of patients with primary hypercholesterolemia.
Gagn&#xe9 - *Am J Cardiol* - 15-NOV-2002; 90(10): 1084-91
From NIH/NLM MEDLINE
Full Text Abstract

Identification and treatment of individuals at high risk of coronary heart disease.
Stein EA - *Am J Med* - 3-JUN-2002; 112 Suppl 8A: 3S-9S
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Review Full Text Abstract

Superior short-term cholesterol control and achievement of the adult treatment panel III low-density lipoprotein goals with initiation of statin therapy by the time of hospital discharge following acute myocardial infarction.
Bybee KA - *Am J Cardiol* - 15-MAR-2004; 93(6): 776-9
From NIH/NLM MEDLINE
Full Text Abstract

Optimizing lipid management in patients with acute coronary syndromes.
Pepine CJ - *Am J Cardiol* - 20-FEB-2003; 91(4A): 30B-35B
From NIH/NLM MEDLINE
Review Full Text Abstract

Statins do not meet expectations for lowering low-density lipoprotein cholesterol levels when used in clinical practice.
Frolkis JP - *Am J Med* - 1-DEC-2002; 113(8): 625-9

Bristol-Myers Squibb Company
P.O. Box 4500 Princeton, NJ 08543-4500

Dear Healthcare Professional:

CHANGES TO LABELING FOR DESYREL® (TRAZODONE HYDROCHLORIDE) TABLETS

Bristol-Myers Squibb Company (BMS) would like to advise you of important package insert changes concerning DESYREL® (trazodone hydrochloride) Tablets. DESYREL is indicated for the treatment of depression. We are writing to inform you that Bristol-Myers Squibb Company, in close cooperation with the U.S. Food and Drug Administration (FDA), has adopted new labeling for DESYREL.

The following label changes include modifications to the **CLINICAL PHARMACOLOGY** section:

> *Metabolism*
> *In vitro* studies in human liver microsomes show that trazodone is metabolized to an active metabolite, m-chlorophenylpiperazine (mCPP) by cytochrome P450 3A4 (CYP3A4). Other metabolic pathways that may be involved in metabolism of trazodone have not been well characterized.
> *Elimination*
> In some patients DESYREL may accumulate in the plasma.
> **Drug-Drug Interactions**
> See also **PRECAUTIONS: Drug Interactions**. *In vitro* drug metabolism studies reveal that trazodone is a substrate of the cytochrome P450 3A4 (CYP3A4) enzyme and trazodone metabolism can be inhibited by the CYP3A4 inhibitors ketoconazole, ritonavir, and indinavir. The effect of short-term administration of ritonavir (200 mg twice daily, 4 doses) on the pharmacokinetics of a single dose of trazodone (50 mg) has been studied in 10 healthy subjects. The C_{max} of trazodone increased by 34%, the AUC increased 2.4-fold, the half-life increased by 2.2-fold, and the clearance decreased by 52%. Adverse effects including nausea, hypotension, and syncope were observed when ritonavir and trazodone were co-administered.
> Carbamazepine induces CYP3A4. Following co-administration of carbamazepine 400 mg/day with trazodone 100 mg to 300 mg daily, carbamazepine reduced plasma concentrations of trazodone (as well as mCPP) by 76 and 60%, respectively, compared to pre-carbamazepine values.

Additionally, the **Drug Interactions** sub-section within the **PRECAUTIONS** section has been updated with the following information:

> *In vitro* drug metabolism studies suggest that there is a potential for drug interactions when trazodone is given with CYP3A4 inhibitors. Ritonavir, a potent CYP3A4 inhibitor, increased the C_{max}, AUC, and elimination half-life, and decreased clearance of trazodone after administration of ritonavir twice daily for 2 days. Adverse effects including nausea, hypotension, and syncope were observed when ritonavir and trazodone were co-administered. It is likely that ketoconazole, indinavir, and other CYP3A4 inhibitors such as itraconazole or nefazodone may lead to substantial increases in trazodone plasma concentrations with the potential for adverse

effects. If trazodone is used with a potent CYP3A4 inhibitor, a lower dose of trazodone should be considered.
Carbamazepine reduced plasma concentrations of trazodone when co-administered. Patients should be closely monitored to see if there is a need for an increased dose of trazodone when taking both drugs.

Healthcare professionals are strongly encouraged to report any serious adverse events that occur with the use of DESYREL to 1-800-321-1335 or to the FDA's MedWatch program by phone (1-800-FDA-1088), fax (1-800-FDA-0178), via the MedWatch website at www.FDA.gov/medwatch, or by mail (using postage-paid form) to MedWatch, HF-2, 5600 Fishers Lane, Rockville, MD 20852-9787.

A COPY OF THE FULL PRESCRIBING INFORMATION FOR DESYREL® (TRAZODONE HYDROCHLORIDE) TABLETS IS ENCLOSED. If you have further questions or require additional information, please contact the Bristol-Myers Squibb Medical Communications Department at 1-800-321-1335.

Sincerely,

Freda C. Lewis-Hall M.D.

Freda C. Lewis-Hall, M.D.
Senior Vice President
U.S. Medical Affairs
Bristol-Myers Squibb Company

Enclosure: Package Insert