Pharmacy and Therapeutics Committee Meeting Record

Date: 10/20/06 **Time:** 9:15 a.m. – 3:15 p.m. **Location:** 3232 Elder Street, Conference Room D

Moderator: Steve Montamat, M.D.

Committee Members Present: Phil Petersen, M.D.; Thomas Rau, M.D.; Steve Montamat, M.D.; William Woodhouse, M.D.; Catherine Gundlach, PharmD; Rick Sutton, RPh; Bob Comstock, RPh; Stan Eisele, M.D., Tami Eide, Pharm.D

Others Present: Selma Gearhardt, PharmD; Steve Liles, PharmD, Bob Faller, Cindy Brock

Committee Members Absent: Richard Markuson, RPh, Donald Norris, M.D.

AGENDA ITEMS	PRESENTER	OUTCOME/ACTIONS
CALL TO ORDER	Steve Montamat, M.D.	Dr. Montamat called the meeting to order.
Committee Business		
➢ *Roll Call*	Steve Montamat, M.D.	Richard Markuson, RPh and Donald Norris, M.D. were noted as absent
➢ *Reading of Confidentiality Statement*	Steve Montamat, M.D.	Dr. Montamat read the Confidentiality Statement
➢ *Approval of Minutes from August 18, 2006 Meeting*	Steve Montamat, M.D.	Dr. Montamat pointed out that on page 5, Patnol is misspelled and needs to be corrected. Minutes were approved with the noted change.
➢ *Resignations*		Dr. Montamat announced his resignation as chair of the Committee. Dr. Eide announced that Cindy Brock would be leaving as administrative support for the Committee.
➢ *DERP II Update*	Tami Eide, PharmD	DERP I still has deliverables to complete. DERP II began in July and will have a new focus. DERP II's focus will be to step out of the traditional role of drug class review. They will look at Neuropathic pain first, drugs for chronic constipation second and combination drugs will be their third area. The group will focus on the place in current therapy for the use of these drugs, in particular pediatrics. DERP II will be a three year project.
Public Comment Period	Steve Montamat, M.D.	22 people signed up to speak during the public comment period. Public comment was received from the following speakers:

Speaker	Representing	Agent	Class
Robert Lee, M.D.	Self	Lipitor	Statins
Dawn King, M.D.	Self	Detrol/Detrol LA	OAB
Ameit Sharma, M.D.	Self	Lipitor/atorvastatin	Statins
Paul Ryan, M.D.	Self	Lotrel	ACE-CCBs
Scott Hiatt, M.D.	Self	Lipitor	Statins
David Henchman, M.D.	Self	Benicar, Benicar HCT	ARBs
Jason Olm	DaiichiSankyo	Wellcol	Lipotropics
Jeff Jenkins	Merck	Cozaar, Hyzaar	ARBs
Neilann Horner	GSK	Rosaglitozone/ Avanda	TZDs
Sylvia Foster, PharmD	GSK	Arixtra—fondaparanex	Anticoagulants
Dr. Roy Palmer	Pfizer	Lipitor	Statins
Dr. Mandy Hoster	AstraZeneca	Crestor	Statins
Dr. Kimmy Moresee	Reliant	Omicor	Lipotropics
Sylvia Foster	GSK	Lotrel	ACE-CCBs
Stephen Stein	Takada	Piloglitazone	TZDs
Sue Heineman	Pfizer	Detrol LA	OAB
Long Nguyen	GSK	Coreg	Beta Blockers
Gerry Shoshita	ScheringPlough	Zetia /Vytorin	Statins
Allen Christie	GSK	Avodart	BPH
Darren Hill	Pfizer	Caduet	CCBs/Statins
Dave Harper	SantofiAvetis	Avapro	Angiotensin 2 Antagonist
Robert Martin	Novartis	Diovan, Starlix, Lotrel	multiple

Drug Class Review

- **Statins**

Steve Montamat, M.D.

Statins—Update #4

Dr. Montamat reviewed five key questions. The focus of the review was on adult patients in both the inpatient and outpatient setting. His review included new clinical

		trial data for outcomes, adverse events, efficacy and safety. The trial data was good quality for diabetics. There was no new evidence to indicate that one Statin was superior over another.
➢ **Lipotropics**	Steve Liles, PharmD	**<u>Lipotropics</u>** Dr. Liles reviewed the new indications for this class, clinical trial data, warnings, drug interactions and contraindications. Many of these agents do not have good efficacy data in pediatric patients. He also reviewed the ATP III Guidelines currently utilized for primary prevention.
➢ **ACE Inhibitors-- Calcium Channel Blocker Combinations**	Steve Liles, PharmD	**<u>ACE Inhibitors/Calcium Channel Blocker Combinations</u>** Dr. Liles reviewed the JNC 7 Hypertension Treatment Guidelines for this class. Treatment is generally the same for all demographic groups. However, socioeconomic status and lifestyle are barriers. There is a higher prevalence and severity in African Americans. These agents are contraindicated for use during pregnancy. He reviewed the indications, pharmacokinetics, and clinical trial data. Drug interactions were similar to those found in individual components. Dosage forms are all once per day medications. The data indicated that better results were achieved from using combination agents than using two individual components.
➢ **Beta Blockers**	Steve Liles, PharmD	**<u>Beta Blockers</u>** Dr. Liles reviewed the ACC/AHA 2005 Guidelines for this class. His review included the four stages of heart failure, the recommendations for ACE Inhibitors, ARBs and Beta Blockers including their use in special population with concomitant disorders. He also reviewed new clinical trial data on the indications, half life of beta blockers, pharmacokinetics, special populations, warnings, contraindications, adverse reactions, and dosage forms. There was no data for pediatrics.
➢ **Angiotensin2 Receptor Blockers**	Tami Eide, PharmD	**<u>Angiotensin2 Receptor Blockers</u>** Dr. Eide reviewed significant data from the last DERP review. ARBs all primarily indicated for hypertension. Some agents have other FDA approved indications.
➢ **Calcium Channel Blockers**	Tami Eide, PharmD	**<u>Calcium Channel Blockers</u>** Dr. Eide presented new data from DERP which included a review of therapeutic indications, unlabeled uses, clinical pharmacology, adverse events, contraindications and drug-to-drug interactions.
Review of Clinical Data—DERP Review		

➢ **Bladder Relaxants**	Marian McDonagh, Pharm.D--DERP	Dr. McDonagh provided the Committee with information on the results for update 3. She presented new clinical trial data on agents with comparative efficacy for this class. No differences were found on a variety of outcome measurements for different formulations. Comparative efficacy showed some significant differences. Withdrawal rates and adverse event rates were significantly lower with the extended release formulations of the agents. Quality of life was significantly improved in patients who used this class.
➢ **Hypoglycemics, TZDs**	Susan Carson, M.D.	Dr. Carson presented comparative data on Pioglitazone and Rosiglitazone. Her review included: efficacy, effectiveness, and adverse events. Data was lacking on long-term effects, comparative effects on weight, effectiveness or quality of life. No significant difference in outcomes on A1c between the two agents.
➢ **Hypoglycemics, Meglitinides**	Steve Liles, PharmD	Dr. Liles reviewed the guidelines for the Management of Hyperglycemia in Type 2 Diabetes. His review also included clinical trial data on Starlix and Prandin. His presentation included the pharmacokinetic properties, warnings, contraindications, drug interactions, adverse reactions, and dosage forms.
➢ **BPH Agents**	Steve Liles, PharmD	Dr. Liles presented a data comparison of agents indicated for the treatment of BPH in men. Clinical data indicated that non-responders to one agent did not respond to another agent and that combination therapy seemed to be more effective. He also reviewed the warnings, contraindications, adverse reactions and dosage forms. Sexual side effects appeared to be more significant for Alpha Blockers compared to 5AR Inhibitors. The AUA 2003 Guidelines indicate that combination therapy is recommended for the treatment of BPH.
➢ **Phosphate Binders**	Steve Liles, PharmD	Dr. Liles reviewed new data since his last review of this class in May 2006. His clinical trial data review included indications, pharmacokinetics, warnings, contraindications, adverse reactions and dosages. This class is not recommended for use in pediatrics. He also reviewed the 2004 K/DOQI Guidelines for treatment.
➢ **Injectable Anticoagulants**	Steve Liles, PharmD	Dr. Liles presented clinical trial data on the indications, pharmacokinetics, warnings, adverse reactions and dosage forms. The incidence of major bleeding was similar with all the agents in this class, but VTE was recommended for the treatment of children.
Committee Clinical Discussions and Conclusions		**<u>Statins</u>** The Committee did not feel there was a significant difference between agents in this class. Generic Simvastatin may become less expensive in January 2006 due to the DRA changes in the Federal Upper Payment Limits and the Committee may want to review their recommendations again at that time. **<u>Lipotropics</u>**

		The Committee felt there was no new data and did not feel the need to make any changes to their recommendations for this class. **ACE Inhibitors/Calcium Channel Blocker Combinations** The Committee would like to see more data on adherence. DERP II will be reviewing this class in the future. None of the combination agents stand out. **Beta Blockers** The Committee felt that adverse effects caused more caution for Coreg in than other agents in this class. Efficacy is a wash. No changes recommended at this time. **Angiotensin2 Receptor Blockers** The Committee would like to have more discussion on the potential for these agents to become a first line agent. Committee did not see any significant differences between the agents for this class. **Calcium Channel Blockers** The Committee felt there was no new data and did not feel the need to make any changes to their recommendations for this class. **Bladder Relaxants** The Committee felt the adherence in this class was not good and the side effect profiles for each agent were significant. Since the implementation of Medicare Part D, the number of prescriptions has decreased in usage and it may not be valuable to the Committee to change preferred agents. **Hypoglycemics, TZD** The Committee felt the new data did not indicate a need to change their prior recommendations. **Hypoglycemics, Meglitnides** The Committee felt that the agents in this class were similar and there was not a clinically significant difference. **BPH Agents** The Committee felt there may be enough data to indicate a preferred agent in this class. Avodart was considered as a candidate for the PDL. **Phosphate Binders** The Committee felt there was no new data and did not feel the need to make any changes to their recommendations for this class.

		Injectable Anticoagulants The Committee's felt there was a need to keep all agents in this class available because of the variance in indications.
Public Meeting Adjourned		Dr. Montamat adjourned the public portion of the meeting and reminded the Committee that recommendations for the classes reviewed today will be made at the February meeting.
Closed Executive Session	Paul Leary, Medicaid Deputy Administrator	No Executive Session was held.

Pharmacy and Therapeutics Committee
Public Comment
October 20, 2006

Robert Lee, M.D.
Good morning. You probably recognize me, because I have been here before and also speaking for the same topic which is Lipitor. I am a private cardiologist here in Boise doing both general cardiology and also interventional cardiology. I just wanted to talk about Lipitor. I wanted to mention that Lipitor is probably my primary drug that I use in the Statin class. The reason for that is I feel quite strongly that it does have very strong data to support its use over other statins and other agents. One thing that I would like to mention is that I have a ton of patients and I think a lot of the practitioners in Boise have a ton of patients on Lipitor. To remove Lipitor from easy access and easy use is going to be extremely onerous. We have found that to be the case with some of the other payors including Blue Cross and Regence where we have to demonstrate that other drugs are not efficacious and that we have tried those already. There is a ton of paperwork with all of them doing that and then you have to write a new prescription for the patient, etc., etc. It is really onerous. I would plead to you for you to allow us to continue to use Lipitor freely. You know, the data to support the use of Lipitor is very compelling. You know, most of the studies that have changed the NCP III Guidelines have been based on the use of high dose Lipitor. We have the ASCOT, CARDS, REVERSAL, and PROVE-IT (which was not even done by Pfizer) Trials and they all support the use of Lipitor. The argument that has been put forward is that there are regression studies and meta-analysis which support all the agents as a class. If you look at these studies, the Lipitor studies were ended early. If you were to continue these studies out to the proposed time, they would probably be significantly superior. These arguments, it is very difficult to this in three minutes. I would really, really plead to you to allow us to continue to use Lipitor freely and without restriction.

Dawn King, M.D.
I am Dawn King. I am a urologist in Boise, ID and I like to think that I have better hair than Don King the boxing promoter. I am here on behalf of several of the urologists in Idaho that could not be here today. I am talking in support of Detrol LA or Tolteradine. This medication has been around for a number of years. It was one of the first ones to come out for the treatment of over-active bladder. They have really revolutionized the treatment of over-active bladder. Before, this medication, we had generic Ditropan, which was not well tolerated in many patients and they would stop therapy, because they couldn't tolerate it. When Detrol and Detrol LA came out, patients saw better results with this medication and it was well tolerated because of fewer side effects such as dry mouth and constipation. This drug has been on and off the formulary now for several years and it has been frustrating for us. It is probably the number one drug that I use, mainly because it is well tolerated. It is a good drug, it works. There are several studies to support it. I'm not going in to those, but there are several studies out there that I have looked at. It has low drug to drug interactions and fewer CNS side effects than some of the other over-active bladder medications. I think that

the frustrating thing for us has been that sometimes it is on the formulary and then it's off. It's on and then off. It's frustrating to have to do the prior authorization and determine if we can use it or we can't. Again, it is one of the number one drugs I will use and I treat a lot of over-active bladder every week. I see 10-20 patients per week that have over-active bladder, so I have a lot of experience with it and I would just strongly recommend that it be added back on the formulary. Thank you.

Ameit Sharma, M.D.
Good morning. I am Ameit Sharma and I am here representing Boise Kidney. I moved into this area a year ago. We have a free nephrology practice here and we are starting to do some research. I am on the Institutional Review Board at Saint Alphonsus. The topic for me is statin use in kidney disease. There are three issues that I want to point out. One is the clinical safety of Lipitor in chronic kidney disease patients. I think the data supports that quite clearly. There are two trials that I want to mention. One is the ASCOT Trial, the Lipid lowering arm, and also the CARDS Trial, which is in diabetic patients. I think that when you look at both of these trials there is a 36% reduction in events from a primary standpoint and then when you also look at the renal data in these patients, it is very important. What we are tending to do and I have just submitted a grant to Amgen to look at algorithm based therapy in investigative or initiated roles. So, we really want to use a titration scheme and we are very comfortable in using the highest dose of certain agents, whether they are ARBs, Statins or insulin agents. The agent that we chose was Atorvostatin, all the way up to 80mgs for kidney disease patients and that is because the safety data in kidney disease, if we look at the Kidney Dialysis Quality Outcome Initiative, is clear that there is no dose reduction in kidney disease. So, for our patients that are in this Medicaid population, I feel that from a safety standpoint, you have to push the dose to get an LDL less than 70 and the only way to do that is by using a high dose Statin. The only two statins that are safe by the Kidney Dialysis Quality Outcome Initiative without a dose reduction are pravastatin and Atorvostatin. So, that's my position. Thank you.

Paul Ryan, M.D.
Thank you. My name is Paul Ryan and I am a family medicine practitioner here in Boise that sees Medicaid patients and my practice is primarily Medicaid patients and I am here to make my request that you keep a combination ACE Inhibitor/Calcium Channel Blocker Lotrel on the formulary. Lotrel is probably one of the few combination medications that I use. Because of its effectiveness, it is something that I use a lot of. Because of its having two medications in one, provides a high level of compliance for a lot of patients that have difficult to control hypertension. It has a very low side effect profile. The incidence of edema with amlodipine by itself, is pretty significant, but when it's combined with the ACE Inhibitor, it is really is much more tolerable for the patients and because of its friendly side effect profile, it has very high level of compliance as well. It is available in quite a number of dosages, so having to flip flop between combining different dosages of medications (which may or may not be on the formulary) becomes fairly onerous at times and to be able to have a medication that is as effective as Lotrel that is so well tolerated is pretty important to my general practice. I really don't have any scientific data to present to you, but I think that in the clinical practice, we know the effectiveness of Lotrel and if you keep it on the formulary, it would be a big boost to avoid the whole process of prior authorization.
Thank you.

Scott Hiatt, M.D.
Good morning. I am Scott Hiatt and I am a cardiologist practicing in Nampa, ID at Mercy Medical Center. I am here on behalf of Lipitor and Pfizer. I don't speak for them and I don't even own any of their stock. I am here to ask you to please leave Lipitor on the formulary. By the time I see patients, they almost all have coronary disease and their LDL goal is 70. This requires frequently potent statin or combination therapy. As it stands, there is just one drug that has long term efficacy and safety data to support its long term use. I hope that the others do someday, but at this point in time they do not. For that reason alone, I think it is important to leave it on the formulary. Just because of the data and the safety that we already know that it possess. Thank you.

David Henchman, M.D.
I am David Henchman, a cardiologist in Boise, with Idaho Cardiology Associates and I see a number of Medicaid patients in my practice and I would like you to consider keeping Benacar and Benacar HCT on the formulary primarily because of its potency and its tolerability. I think we still continue to do a pretty poor job

at keeping patients at their blood pressure goals and we know that the majority of patients in our practice still struggle to hit target blood pressure levels of 120/80, even on multiple agents. I have found that Benacar and Benacar HCT are potent enough to be able to eliminate a number of other medications that may produce other side effects and I have been able to go to this single agent frequently, because it is very effective at lowering blood pressure. It has a very clean side effect profile. We watch for hyperkalemia, but that is extremely rare and aside from that, it is extremely well tolerated without a lot of side effects. If you then add a hydrochloriciozide component in the form of Benacar HCT that pushes the potassium levels down when Benacar may be raising them and you usually end up with a net neutral effect on potassium. So, I think that it is a very well tolerated drug. It's a very potent drug. My favorite part is that in these patients that are on multiple medications, I find that I can usually drop one or two other agents by going to this single agent. I hope that it would stay on the formulary. Thank you.

Jason Olm

Good morning ladies and gentlemen of the committee. My name is Jason Olm and I am a medical liaison with DaiichiSankyo based out of Seattle, WA. I am here today to testify on behalf of Welchol, which is also known as cholohydrochloride. Welchol is a non systemic, lipid lowering, bile acid sequestriant. It's indicated as adjunctive therapy to diet and exercise for the reduction of LDL cholesterol in patients with primary hypercholesterol anemia. Welchol binds bile acids and impedes their active transport and reabsorption and enhances fecal bile acids excretion. With regard to efficacy, Welchol at the starting dose of 3.8g daily and the maximum dose of 4.5g daily resulted in a statistically significant 15 and 18 percent mean reduction in LDL cholesterol. These LDL cholesterol reductions were observed within the two weeks following treatment and were maintained during the long term therapy over a 24 week period. With Welchol, changes in triglycerides were approximately 5% higher in patients, which was not significantly different when compared to placebo. Combination treatment with Welchol at 3.8g per day and Lipitor at 10mgs per day resulted in a significant decrease in the mean LDL cholesterol concentration of 48% and a total cholesterol reduction of 31%. Welchol, in combination with Lipitor at 10mgs daily provided an LDL cholesterol reduction similar to that of a high dose of Atorvostatin without the extra systemic risk. Welchol is contraindicated in individuals with bowel obstruction or those with hypersensitivity to any of the components. Caution should be exercised when treating patients with dysphasia, severe GI motility disorders or major GI tract surgery and when treating patients with triglyceride levels of greater than 300mgs per deciliter, as bile acid sequestrants are known to increase triglyceride levels. In a post marketing experience with Welchol, rare incidences of elevated TSH levels were reported in patients taking Welchol in concomitant with that of thyroid hormone replacement. Welchol has not been studied with all drugs and when administering a drug with a narrow therapeutic index or a margin of safety that has not been evaluated in a formal drug to drug interaction study, the drug should be administered at least one hour before or four hours after Welchol or consider monitoring blood levels of the drug. The most common side effects with Welchol versus that of placebo are flatulence, constipation, infection, dyspepsia, and headache. Conveniently, Welchol requires no additional liver monitoring as monotherapy and does not recommend any additional liver monitoring after concomitant use with statin therapy outside of what the statin recommendations are. In addition, Welchol is one of the few lipid lowering agents classified as pregnancy Category B. Welchol is a non systemic agent, with convenient dosing, and is indicated for LDL cholesterol lowering as monotherapy or in combination with a dose of a statin. It is important that patients have access to Welchol, because the most recent NCEP III Guidelines recommend an LDL cholesterol goal of less than 100mgs per deciliter or an optimal more aggressive goal of less than 70mgs per deciliter for the high risk populations and most of these patients will require multiple medications to achieve these aggressive targets. Thank you for your time.

Jeff Jenkins

Good morning. My name is Jeff Jenkins and I am a senor national account executive with Merck. I have been with Merck for 25 years and it's hard to believe. I'm here pitch hitting for Bob Calder our Medical Director who couldn't make it down here today from Wisconsin. He was tied up. He addressed you the last time in March when you reviewed the ARB class. I am going to limit my comments to really three points and they line up well with our indications and with some of the questions in the Oregon report which I believe you will review later today. The first point is in the ARB class, there are really no head to head comparisons with the drugs in this class. They are all indicated for hypertension, so hypertension is really the common point that all these drugs have. Our drug is Cozaar. Another point of commonality is that they are all available in combination with hydrochlorothiazide. They all have a box warning for use during pregnancy. That has been in the label for all of these drugs for a long time. My second point, the indications for diabetic nephropathy, Cozaar is indicated for the treatment of diabetic nephropathy and this was a result of the Ranal Study that published in 2001 in the New England Journal of Medicine by Dr. Brennar and

they studied Cozaar versus placebo and they were studying the doubling of serum creatinine in end stage renal disease and death. What was found in Ranal and is in our label and is in the Oregon report as well, is that there was a 16% risk reduction in the primary end point, which was those three combined end points. Now, there was no reduction in death in that particular study, but that was a major study that was shown in the treatment of diabetic nephropathy with Cozaar. The third indication is to reduce the risk of stroke in patients with hypertension-left ventricular hypertrophy. This was reported in a wide study in Lancet and in that study, which studied 9,100 patients, what you found there was a 25% reduction in stroke with Cozaar compared to atenolol, which was the active comparator. They all showed a reduction in blood pressure, so what you will see in the indications section of Cozaar is the only ARB that is indicated to reduce stroke and that will be differentiated in the Oregon report, I believe in Table 2. So, Cozaar is currently on the Preferred Drug List in the State of Idaho and we appreciate that. Based on the evidence, I would ask you to maintain Cozaar and Hyzaar on the PDL. If you have any questions, I would be happy to address them. Thank you.

Neilann Horner

Good morning everybody. I am Neilann Horner and I am in research and development for rosiglitazone with GlaxsoSmithKline. I am here to present a pretty substantial update on data available on Avandia and also to request that Avandia in combination products with metformin and branded Amaryl remain on the PDL. Avandia, as you are probably aware, is an insulin resensitizer that addresses both the core defects in Type II diabetes, both insulin resistance and beta cell dysfunction. While both TZDs currently on the market only have an FDA indications for treating Type II diabetes as an adjunct to diet and exercise, the scientific basis that I understand you're working with the OHSU report that reviews this class of drugs, poses eight key questions to us. Four of those are to off label use for prediabetes or metabolic syndrome. So, today, I just wanted to make you aware that as of September 15th a landmark trial reported with 5,200 patients called Dream, affectionally. It was a diabetic assessment with ramapril and rosiglitazone medication. It is a 2 by 2 factorial design that is able to look at the independent effects of each of those drugs. I am only going to address the Avandia arm, but a median follow up of three years in an impaired glucose intolerance crowd with an impaired fasting glucose, so the glucose range is just prior to the cut off for diagnosis of Type II diabetes are who is in this trial. The primary input being new onset of Type II diabetes, plus death. It is not a mortality trial. The death is in there to try to capture those that might have died without knowledge of them developing diabetes, so it is a numerator and denominator just as a way to capture all diagnosis. A 60% reduction in new onset Type II diabetes was found with 8mgs daily of Avandia versus placebo in this group. It is currently still ethical to have no drug therapy in metabolic syndrome and Prediabetes since we have no standards to date. So, that was rather novel information. To further go on to tell you a little bit more about that, the absolute numbers, which is helpful hopefully, 10.6% developed diabetes in the treatment group versus 25%. That is a difference between 280 patients and 658 that went on to develop diabetes. There was likelihood of 70-80% more likely to revert to normal glycemia on Avandia. So, taking them out of that prediabetic range and returning them to normal glycemia also. If one were to treat a thousand patients for three years, there would be an opportunity to prevent a 144 cases of Type II diabetes with an excess of four cases of heart failure. That's in Lancet, September 23rd, for your review in a peer review fashion. I thank you for your time and I will take questions if you have any.

Sylvia Foster, PharmD

Good morning. I am a pharmacist and I spent 10 years as an anticoagulation specialist at a community hospital and recently work on the behalf of GSK primarily for the clinical education and research of fondaparanex, also known as Arixtra, which is one of the newest anticoagulants. First I want to emphasize that fondaparanex is not a low molecular weight heparin. It's the first of the new anticoagulant class of drugs known as Factor 10A Inhibitors. There are several other Factor 10A Inhibitors in development, but Arixtra is the only one available. So what makes Factor 10A Inhibitors different from the low molecular weight heparins? Well, basically it is the mechanism of action. It takes the anticoagulant part of low molecular weight heparins and eliminates all the side chains that can cause some of the problems that come with low molecular weight heparins. Such as, the incidence of heparin induced thrombocytopenia and some of the variability you get in pharmacodynamic response. It's a synthetic molecule, where as the low molecular weight heparins are extracted from the intestinal mucosa of pigs. So, because it's synthetic, it doesn't have the tendency for allergic reactions like heparin and like the low molecular weight heparins can have. It's very potent and has a very quick onset of action. You get anticoagulant activity within 2-3 hours and it has a longer half life, so it only needs to be dosed only once daily in all indications whereas the low molecular weight heparins sometimes they are dosed once per day and sometimes twice a day. The dosing regimen for fondaparanex is very simple. It's always once per day. It's ideal for outpatient use in this way. They are prefilled syringes. The dose of prevention of DVT and

PE is 2.5mgs, once per day and the dose for treatment of DVT and PE is 5, 7.5 or 10mgs once per day depending on where you fit in the weight group. Again, they are prefilled syringes. Each one is color coded to prevent dosing and medication errors and they all come with an information box similar to lovenox to help educate patients when they use it on an outpatient basis. Price wise, it is pretty much equivalent to the low molecular weight heparins. The main difference is that fonadparanex costs the same across the board for treatment no matter how much you weigh with the low molecular weight heparins, the more you weigh, the more is costs. So, anyone who weighs say more than me end up paying more for the low molecular weight heparins than they would for fondaparanex. Indicated for the prevention of DVT and PE, we are the only anticoagulant that is indicated for hip fracture surgery and indicated for the treatment of DVT and PE and we are the only one indicated for the outpatient treatment of PE. We have several studies that are available on other uses. It has been granted priority review by the FDA for the submission for the use in acute coronary syndrome. That is not an outpatient use, so it will not directly affect Medicaid usage, but because of this, more and more hospitals are starting to use fonadparanex and so indirectly, that leads to more and more outpatient prescriptions for fondaparanex. Any questions?

Q: Dr. Montamat asked that as far as cautions or contraindications, can you go over those?
R: First of all, all the anticoagulants have a black box warning with neurolaxial anesthesia. That is common for all. It's contraindicated in prevention only for patients who weigh less than 50kgs. You can use it in patients who weigh less than 50kgs. for treatment and then the renal insufficiency and I know this was brought us last year, anyone with patients with a creatinine clearance of less than 30mgs per minute it is contraindicated in patients for the treatment of DVT. There is more data that is coming out. Primarily in the treatment of acute coronary syndrome setting where they have a lot of data of its use in renal failure. Hopefully, we will get further with that.

Q: Dr. Gundlach asked, what is the deal with thrombocytopenia?
R: Heparin induced thrombocytopenia? \
Q: Say you have someone that has been on lovenox or whatever and their platelets drop to 60,000, use Arixtra?
R: We are not indicated for the treatment in heparin induced thrombocytopenia, but it is currently, besides the direct thrombin inhibitors, the only anticoagulant you can use if it is heparin induced thrombothrombocytopenia. You know that heparin and the low molecular weight heparins are contraindicated if the patient has HIT.
Q: It gets murky, because you're labeling says if your platelets are less than 100,000, you are not supposed to use it.
R: Right, but let's differentiate thrombothrombocytopenia from heparin induced thrombothrombocytopenia. So, if it's general thrombothrombocytopenia it's a caution that anyone with low platelets will have a higher tendency for bleeding if they use an anticoagulant. So, pretty much all the anticoagulants say that if your platelets drop to less than 50,000, you need to use caution when you are using an anticoagulant, because they are at a higher risk of bleeding. That is separate from heparin induced thrombothrombocytopenia where if you have HIT, you want to use a direct thrombin inhibitor such as agatrapan, leparudin, valarudin for the treatment of HIT, but fondaparanex can be used once the HIT has been resolved, where as you still can't use the low molecular weight heparins.

Roy Palmer, M.D.
Good morning. My name is Dr. Roy Palmer and I am part of the Pfizer medical team and I'm here to talk about Lipitor and Atorvostatin. The first thing that I wanted to emphasize is the critical importance of heart cardiovascular end points in assessing the efficacy of a statin. You know, you really don't know what a drug does until you examine it over long periods of study in all different types of patients and see what it does to MIs and strokes. That's ultimately what we want to measure with a statin. With Atorvostatin, we have published data from over 80,000 patients in our clinical trial database and that's primary, secondary prevention, acute coronary syndrome, diabetic patients, and patients with stroke. Pretty much anyone that would get a statin in clinical practice has been examined in great detail in a long term study. In fact, the NSAID, ATP3 recommendations for lower goals were based primarily upon data with Atorvostatin over the last few years. So, not only does that give us a very clear characterization of the benefit, but it allows us to look very carefully at the safety. We have over 80,000 patients in our safety database, most of who have been treated for over three years. In fact, at the highest dose of 80mgs, we have 14,000 patients that we have carefully evaluated and many of the other statins don't have a lot of data at the highest doses. We have carefully evaluated that in many long term studies and the safety has been excellent and there is no evidence of a dose response in our safety relationship with adverse events. There are two particular

patient types that I would like you to consider. One is the acute coronary syndrome patient. The best data that exists is with a Atorvostatin in the Miracle studies. The only other large study looking at that population was not a successful study. So, many physicians believe that the only evidence based choice in these patients is 80mgs of a Atorvostatin. These are obviously a high risk patient population treated as outpatients, once they get out of the hospital. The other patient population that I would like you to consider is stroke patients. The only clinical study evaluating people who have already had a stroke is the Sparkle Study, which we published this August in the New England Journal of Medicine. The only other data on these patients has been a sub analysis of HPS, which showed no benefit with treating with cymbastatin. So, there are two patient populations there where the only positive data has been with a Atorvostatin and the other studies have not shown a benefit. So, I would like you to consider that as what agent you are comfortable with these patients being put on in the State of Idaho. What I am asking you to consider is to weigh the outcomes data, weigh the long term safety data and I would like to consider reinforcing your decision of last year to keep Atorvostatin on the Idaho PDL. Thank you very much.

Mandy Hoster, M.D.

Good morning. My name is Dr. Mandy Hoster. I am a cardiovascular medicine liaison with AstraZenica in Salt Lake City and I would like to thank the committee members for having me here this morning to discuss Crestor with you. Crestor has been on the market for over three years and as of October 10th, over 8 million patients have been treated with Crestor and that has resulted in roughly 61 million prescriptions. In recent years, as we have heard from Dr. Palmer and Dr. Sharma and Dr. Hiatt previously, LDL goals have been lowered to achieve cardiovascular event reduction in patients treated to lower LDL levels. I would like to describe to you how Crestor can help more Idaho Medicaid patients get to that goal. In head to head comparisons with other statins, Crestor lowered cholesterol significantly more on a dose per dose basis. LDL reductions are commonly within the range of 45-63% at the dose range of 5-40mgs, with greater than 50% reduction at the usual 10mgs starting dose. Dr. Lee and Dr. Hiatt both spoke on having to use high dose Lipitor to achieve profound LDL reductions and we can see that with Crestor at the low 10mgs starting dose. In respect to HDL, if that's important and we do believe it is, although we will have more data on that from The Lipitor company soon, Crestor's ability to raise HDL shows an 8-14% increase and it is as effective as Atorvostatin at lowering triglycerides. Crestor is water soluble. What does this mean? It means that it requires minimal metabolism. What does that mean? It doesn't interact with antibiotics or other pharmaceuticals that cardiovascular risk patients might be on for example a calcium channel blocker. With a half life of 19 hours, Crestor can be administered anytime of day, with or without food. The safety of Crestor is not different from those of other currently marketed statins and this was supported by a comprehensive independent safety review by the National Lipid Association, published this year in the American Journal of Cardiology. Dr. Palmer and Dr. Lee spoke very nicely about outcomes data with statins looking at the ASCOT and the CARDS populations. In terms of Crestor's commitment to cardiovascular research in the outcomes area, Crestor's ongoing clinical trial program is called Galaxy. This contains more than 70,000 patients and is being run in over 50 countries. At this time, cardiovascular event outcomes trials for Crestor have been published in the areas of arthrosclerosis regression. Again, currently looking at an acute coronary syndrome patient population. These are patients that enter the cath lab with chest pain, acute coronary syndrome and randomized into a trial with Crestor 40mgs over two years to assess changes in the volume of coronary artery atherolin. It was achieved with a good safety profile, so regression was observed in a statistically significant fashion and this has not been seen in other large statin trials thus far. So, this was a landmark trial for arthrosclerosis regression. This was achieved again with good safety, but it should be noted that Crestor nor any other statins or lipid lowering therapies are indicated for atheroma reduction and the starting dose for Crestor again is 10mgs, although the 40mgs dose was used in that trial. Further cardiovascular event trials are under way for Crestor in different secondary prevention populations that include patients with heart failure with ischemic/idiopathic origin and there is also a trial ongoing in patients with ongoing end stage renal disease, to address Dr. Sharma's interest in this very high risk CKD population. Currently, a primary prevention trial called Jupiter is in the enrollment phase, looking at patients with elevated HSCRP and a chronic inflammatory state, but normal LDL to determine whether or not that would prevent cardiovascular events in that population. Currently, Crestor is approved on 40 Medicaid formularies. Thank you for allowing Crestor to be available to your Idaho Medicaid patient population. Are there any questions? Thank you.

Kimmy Moresee, M.D.

Hi, my name is Dr. Kimmy Moresee and I am from the medical affairs department at Reliant Pharmaceutical. Today, I will be highlighting some key features of Omicor. Omicor is the first and only prescription Omega III fatty acid. It's currently FDA approved for the treatment of triglyceride above 500mgs per deciliter. Omicor has also been shown to be effective in patients with triglycerides betweens 200 and 499 and Reliant has an approval letter from the FDA for this

indication, which we hope to have sometime next year. 4gms per day of Omicor was assessed in two randomized, placebo controlled studies, in patients with average triglyceride level of 880mgs. A 45% reduction was seen in triglyceride levels and a 14% reduction in non HDL levels and a 9% increase in HDL. Omicor does present a new class of triglyceride lowering drugs and does have an alternative mechanism of action and does not have any contraindications or warnings about concomitant use with other drugs. No warnings exist on the label and no serious adverse events have been reported in any Omicor trials. The only statistically significant side effect relative to placebo was taste perversion, which was reported by 6 in 226 patients taking Omicor. Drug to drug interactions due to cytochrome P-450 metabolism are not expected. This drug is rapidly absorbed into the cellular membranes and therefore does not interfere with P-450 activity. Omicor is over 90% concentrated, Omega-3 fatty acid and is derived from wild fish. Each one gram capsule contains 84% EPA and DHA, which are the beneficial fatty acids associated with Omega-3 benefit. So, what distinguishes Omicor from Omega-3 dietary supplements? Well, Omicor is the only FDA approved, Omega-3 monitoring product. Dietary supplements are not approved as a drug and are regulated as a food. This means that they are not required to provide evidence of safety or efficacy to support their claims. Omicor is indicated by the FDA as a treatment for hypertriglyceridemia. Supplements are not intended to be used for the treatment or cure of any disease. The manufacturing process for Omicor continues to be monitored by the FDA. The FDA does not monitor dietary supplements, so no guarantees can be made regarding batch to batch consistency of ingredient amounts, concentration or capsule breakdown packaging. This may pose a risk to the patient and they may not be getting the right amounts of DHA and EPA and may be ingesting environmental toxins such as mercury. The final concentration of EPA and DHA in Omicor is 84%. Dietary supplements claim they contain 10-50% of EPA and DHA, so to achieve a therapeutic dose a patient might need to take anywhere from 8-20 capsules of supplements to equal the label dose. So, the question arises that if 20 capsules provide around 4gms of pure EPA and DHA, what is the remaining 16gms? There are definitely some calories and some fat, but possibly some other things, such as proinflammatory fatty acids. Because of the limited monitoring, the label may not match what is actually in the bottle and once again supplements are not indicated for the treatment of disease. Omicor allows the physicians to appropriately dose Omega-3 fatty acids for the safe and effective treatment of hypertriglyceridemia, without the risk of unwanted byproducts. On behalf of Reliant Pharmaceuticals, I would like to thank you for the opportunity to present at today's meeting and I will take any questions.

Q: Dr. Gundlach asked for information on the use of Omicor in pregnant patients.
R: We are pregnancy category C. We have no data for pregnant patients.
Q: You are not doing any studies?
R: We are not currently doing any studies.
Q: Isn't there some data about Omega-3 fatty acids in prenatal vitamins?
R: Yes, there is and actually they are putting some of the Omega-3s into some of the prenatal vitamins, but our company currently is only marketing it for hyperglyceridemia. We may look at that down the road, but not right now.
Q: Dr. Woodhouse asked about their heavy metal content.
R: We know that our own heavy metal content is undetected.
Q: What kind of fish do you use?
R: We use anchovies, herring and macrel.

Public comment was also received from Sylvia Foster, Stephen Stein, Sue Heineman, Long Nguyen, Gerry Shoshita, Allen Christie, Darren Hill and Dave Harper but due to technical issues their testimony was untranscribable.