Pharmacy and Therapeutics Committee Meeting Record

Date: 6/18/04 **Time:** 8:00 a.m. – 10:00 a.m. **Location:** 3232 Elder Street, Conference Room D **Moderator:** Thomas R. Young, M.D.

Committee Members Present: Thomas R. Young, M.D.; Richard Pines, D.O.; George Pfoertner, M.D.; Catherine Gundlach, PharmD**;** Jeffery Edwards, M.D., Richard Markuson, RPh**;** Bob Comstock, RPh; Thomas Rau, M.D.; Rick Sutton, RPh; Shawna Kittridge, MHS, RPh; Steve Montamat, M.D.

Agenda Item	Presenter	Outcome/Action	Assigned	Due
CALL TO ORDER • **Roll Call** • **Reading of Confidentiality Statement**	Thomas R. Young, M.D.	Dr. Young called the roll. The confidentiality statement was read by Dr. Young.		
REVIEW OF CLINICAL DATA • **Statins**	Mark Helfand, M.D., MPH	Dr. Helfand attended via conference call and highlighted updates to key questions and content of the statin EPC report. This report is the "Updated Final Report #2" dated June 2004. A copy of the report was included in Committee member packets.		
Public Comment Period	Thomas R. Young, M.D.	Public comment was received from the following: • Speaker 1 - Dr. Herb with Astra Zeneca • Speaker 2 - Richard Ennsin representing Pfizer.		
COMMITTEE RECOMMENDATION FOR SELECTED THERAPEUTIC CLASS	Thomas R. Young, M.D.	Statins The Committee's recommendations for the Statin drug class based on clinical evidence are that at least one of the "High Potency" drugs (Lipitor®, Crestor® and Zocor®) should be selected as preferred agents. In addition the Committee recommends that Crestor® should not be the only "High Potency" drug selected due to long term safety concerns. Additionally it is recommended that Pravachol® be selected as a preferred agent due to its safety record.		
SUPPLEMENTAL REBATE INFORMATION (CLOSED TO PUBLIC)	Shawna Kittridge, MHS, RPh	Shawna Kittridge presented cost models based on supplemental rebate and Idaho Medicaid utilization information to the Committee members for their review and discussion. This review and discussion was closed to the public.		
COMMITTEE FINAL RECOMMENDATION FOR THERAPEUTIC CLASSES	Thomas R. Young, M.D.	Based on the clinical evidence, utilization and cost modeling the Committee recommends that Lovastatin, Lescol®, Lescol XL®, Altocor®, Advicor®, Lipitor®, Crestor®, Pravachol®, and Zocor® be considered preferred agents.		
ADJOURN COMMITTEE MEETING	Thomas R. Young, M.D.	Dr. Young adjourned the meeting.		

Pharmacy and Therapeutics Committee
Public Comment
June 18, 2004

Dr. Herb: Thank you for your time and I appreciate the review by the previous speaker. I did have a couple of comments to clarify some things on terms of the questions the committee had. One if you look at table two which had been discussed quite a bit in terms of comparisons of rosuvastatin versus any other statin, I want to make sure that you are aware of the fact all five of those trials have been published. Those are not [inaudible] file. Those are now on the public domain and I want to make sure that's clear that those were published in 2002 – 2003. Further, of studies 25 and the Olsson are all published as well as the unnamed one that that you see listed there [inaudible].

The Jones trial is the largest comparative trial ever inducted, comparing the currently marketed statins. And that the sample size for that was over 2200 patients. With possibly four to six hundred patients per statin across their dosing ranges [inaudible].

Shawna Kittridge: Could you hold a second Dr. Herb?

Dr. Herb: Sure!

Shawna Kittridge: Go ahead Mark.

Mark Helfand: I just wonder, we did not find a journal publication just about study twenty-five. We found two meta analogies that included information from it, but did we miss this very reference for the published version of study 25?

Dr. Herb: Yeah, I can provide it to you off line if you would like, but I don't want to use my time, [inaudible] but I needed to provide you with a reference.

Dr. Young: Could you just tell us what publication it was in?

Dr. Herb: Okay, I just pulled it up a minute ago. It was probably of the highest thing. I don't memorize the citations. The Olsson trial was published American Journal (American Heart Journal) December of '02.

Dr. Young: With the Olsson in study 26, is there two Olsson's?

Dr. Herb: Yeah, there's more than one.

Dr. Young: Okay, then what was that again you just said it was?

Dr. Herb: American Heart Journal of 2002. December 2002. [inaudible]

Specific to the questions of the Committee, what about the percent of patients using 40 mg. dose of Crestor? You want the utilization rate subsequent to its release worldwide. You've got over 1.8 million patients on the medication with over 4.4 million prescriptions currently. The utilization rate of the 40 mg. dose is less than 4 percent. So it's very low. And the reason that it's very low is because as the most efficacious statin on the market you don't need the higher dose to achieve goal whether it's a high risk or relatively lower risk patient. So that greater utilization per the question is quite well.

The other thing that I would like to through out there in terms of safety, a couple points: One, all statins have interaction with cyclosporin. It is not unique to rosuvastatin. We give guidance in our label, that patients on rosuvastatin should not be taking more than 5 mg. It's

based on some follicle, kinetic, and dynamic studies that were done as part of our approval process. I would also point out that gemfibrazol interaction, rosuvastatin is not unique. That all statins have interaction with gemfibrazol, ranging from two to three full increases in systemic exposure or area on the curve. The outlier of that would have been cerivastatin**,** but all statins have a high prevalence for irrationally [inaudible]. The rational for the 80 mg. dose if upon approval really was looked at a risk/benefit analysis and it turns out that if you were to compare the risk/benefits analysis of the atorvastatin 160 or cerivastatin 160 which have been [inaudible] you would probably see a similar profile. Regarding the Japanese/ Chinese question which came up. It was interesting that the pharmacokinetic profile would the inpatients that ethnicity in other countries demonstrated that there was increased systemic exposure. If you were to look at the labels and doses available in Japan for example, you would see that they were half of what they are in the U.S.

The United States label raise flags for a cerivastatins, who are marketed all doses of statins that probably reflect not a uniqueness on a pharmacokinetic interaction where ethnicity of these Asian patients, but one that is probably related to the class.

We do have as the previous presenter mentioned, we do have an ongoing trial called the Aries trial, which is being run to evaluate the pharmacokinetic as well as dynamic influences for rosuvastatin on that patient population. So we have been as best we can proactive at addressing that. Let's see….

I think it's been very clear that the previous presenter talked a lot about *Lower is Better*, and *PROVE-IT*, and *Reversal* and other trials have further substantiated that in [inaudible] and point trial.

The July circulation, this July's circulation will provide that white paper, and I think that you will be I don't think surprised but I think that it's going to be pretty clear that the targets for LDL cholesterol are going to be greatly reduced in the range of 50 – 70 mg. per deciliter. And I think it's clear that given the efficacy of rosuvastatin at a low dose, you can achieve the unset guideline goals in patients at a greater percent across the dose range than any other statin.

And the only other thing that I probably point out is, is the questions about proteinurin that were brought up. I think we have to separate the questions of proteinurin from the more important questions of long term renal safety, since people need to evaluate proteinurin in the context of what it is or what it is not. I shall also point out that it is in several proteinurin or should I say specifically microalbeumin and hematuria are listed as potential side effects and so are all the marketed statin PI"s. And we had just published a paper looking at patients that were either not or were positive protein in their urine or up to 3.8 years, and when you look at final renal function, that is GFR's or glomerial filtration rate and/or creatinine clearance what you see is whether or not a person was proteinurin on rosuvastatin or any other statin. That their GFR's improved and that their creatinine clearances were not compromised.

So I'll say thank you for your time. I'd be happy to address any questions. I just want to make sure that the current information regarding rosuvastatin as the newest statin to the market are addressed. And recognize that we do not have mortality or morbidity trials no statin coming to market ever has in fact…

Dr. Young: Dr. Herb time.

Dr. Herb: Thanks.

Dr. Young: Shawna, next speaker.

Shawna Kittridge: Next speaker is Richard Ennsin?

Richard Ennsin: Ennsin

Shawna Kittridge: Ennsin, with Pfizer

Richard Ennsin: Greetings, it's nice to be able to see a couple of people face to face. Can you hear me alright on the conference call?

Dr. Young: Yes

Richard Ennsin: I'm glad the dogs went after me as well.

My name is Richard Ennsin. I'm a clinical pharmacist with Pfizer in their education and outcomes research division. And I appreciate the opportunity to take a couple of minutes. I'd love to go over some of the outcomes trial and expense of detail, but for time and for your sanity, I think I just want to leave you with a couple points.

The first is, the feedback from the providers in the area here, is that they would like to have access to a potent statin. To be able to use first line to get their patients cholesterol down and give a reduction in events that is shown in the trial. I think Dr. Helfand has given us, you know a hundred and eighty-seven pages of excellent evidence that these statins work.

The question is how do we get them to work in our patients?

Even right now with the LDL goal for high risk patients of less than 100, only a third of patients across the country are given the goal. If we know next month these goals are going to be lowered, it's going to be harder to get there. So, we need to be able to start with a very potent drug upfront, to be able to get the patients to goal. As a pharmacist, I have an interest in compliance and adherence and how do we keep patients on medications. And the more we have to titrate and adjust and jump through hoops, the harder it is.

One thing I found coming from the VA prior to industry is. We would discharge patients on a statin at a particular dose and a particular drug with the instruction to titrate, and they'd come back one, two, three years later, on the same drug, on the same dose. Unfortunately, it doesn't happen.

My first point is we need to be able to choose a potent statin first line to be able to get the reductions we need. As you would expect, you know my recommendation to the board would be that you consider atorvastatin as that statin. And really based on the evidence, there's really a triad of evidence. You have the outcome studies, both in reducing cardiac events. But the big change since you last met is now head to head study. Head to head studies show under that additional reduction, atorvastatin compared to pravastatin reduces events more. But I think on the other hand you have to look at the safety data. And with the years of experience with atorvastatin, there just recently was published a study looking at the composite trials of almost ten thousand patients, and the low risk of adverse effects. Maybe you have with that the FDA data. Dr. Helfand refers to that on page 31 of his report. That with years of clinical experience and millions of patients, you know the outcomes that you're going to get with atorvastatin.

The last thing is the flexible dose. The fact that you can start at different doses. We may not know what the goal is going to be, but if you know what the patient baseline is and when the new recommendations come out, we know what the targets going to be, you can pick the dose to start with that going to get the patients to goal.

So I'll kind of wrap up and just with one comment. The providers in the area, they could of have shown that by using atorvastatin in about 60% of Medicaid patients. They are using it as their work horse to give the cholesterol reduction, to give the events that we need. So I ask

that we continue to do that, give them that option. I think really the next step, it's so hard to identify these high risk patients to get them on a drug and to get them to goal, then we need to make that as easy as possible. And then take the next step and work on adherence. How do we keep the patients on a medication to really get these outcomes we want from the studies.

So for the sake of time I'll stop there and address any questions that you have.

Dr. Young: Shawna?

Shawna Kittridge: Yes?

Dr. Young: Who's next?

Shawna Kittridge: Change of tape, lost response.

Speaker #3: We will take a pass.

Shawna Kittridge: They have declined comment.