Pharmacy and Therapeutics Committee Meeting Record

Date: 11/19/04 **Time:** 9:00 a.m. – 4:00 p.m. **Location:** 3232 Elder Street, Conference Room D **Moderator:** W. Terry Gipson, M.D.

Committee Members Present: W. Terry Gipson, M.D.; Bob Comstock, RPh; Catherine Gundlach, PharmD; Cindy Bunde, P.A, George Pfoertner, M.D.; Jeffery Edwards, M.D.; Richard Pines, D.O.; Richard Markuson, RPh; Rick Sutton, RPh; Selma Gearhardt, PharmD; Steve Montamat, M.D; Thomas Rau, M.D.

Agenda Item	Presenter	Outcome/Action
CALL TO ORDER	W. Terry Gipson, MD	
• **Roll Call**		Dr. Gipson called the roll. All voting and non- voting members were present.
• **Reading of Confidentiality Statement**		The confidentiality statement was read by Dr. Gipson.
• **Approval of Minutes from September 17, 2004 Meeting**		The minutes from the September 17, 2004, Committee meeting were approved.
• **Review of ARB and Beta Blocker Proposals**		The ARB and Beta Blocker Proposals were not reviewed do to unavailability of valid utilization data in time for meeting.
• **Report on October Governance Meeting**	Dr. Eide	Dr. Eide gave a brief background regarding the Governance Group and a report on the meeting attended by her and Dr. Gipson in October 2004.
• **New England Journal Report**		Dr. Eide informed the members that a report appeared in the New England Journal regarding Prior Authorization programs. Idaho was favorably mentioned.
DUR SYNAGIS PRESENTATION	Chris Owens, PharmD	Dr. Owens presented data on the cost, utilization, and prior authorization of Synagis. The results showed a considerable cost savings as a result of the PA process without risk of increase in RSV cases and hospitalization.
DRUG CLASS REVIEW	Tami Eide, PharmD., BCPS, FASHP	
• **Second Generation Anti-depressants**		Dr. Eide presented a review of second generation anti-depressants including indications, how the drugs work, the drug-drug interactions, availability, and dosing. This review included the following drugs: • Citalopram (Celexa®) • Escitalopram (Lexapro®) • Fluoxetine (Prozac®, Sarafem®) • Fluvoxamine (Luvox®) • Paroxetine (Paxil®, Paxil CR®) • Sertraline (Zoloft®) • Venlafaxine (Effexor®, Effexor-XR®) • Bupropion (Wellbutrin®, Wellbutrin SR®, Wellbutrin XL®, Zyban®) • Mirtazapine (Remeron®)

		• Nefazodone
DRUG CLASS REVIEW • **Second Generation Anti-histamines**	Tami Eide, PharmD., BCPS, FASHP	Dr. Eide presented a review of second generation anti-histamine agents including indications, how the drugs work, the drug-drug interactions, availability, and dosing. This review included the following drugs: • Cetirizine (Zyrtec®) • Desloratadine (Clarinex®) • Fexofenadine (Allegra®) • Loratadine (Claritin®, Tavist ND®, Alavert®)
CLINICAL DATA REVIEW • **Proton Pump Inhibitors**	Susan Carson, MPH	Ms. Carson attended via conference call and presented the Oregon Evidence-Based Practice Center's report comparing the proton pump inhibitor drug class. This report was updated in April of 2004. The Committee accessed and reviewed a copy of the report prior to the meeting.
CLINICAL DATA REVIEW • **Second Generation Anti-histamines**	Susan Carson, MPH	Ms. Carson attended via conference call and presented the Oregon Evidence-Based Practice Center's report comparing the second generation anti-histamine drug class. This report was finalized in November of 2004. The Committee accessed and reviewed a copy of the report prior to the meeting.
PUBLIC COMMENT PERIOD – SESSION ONE	W. Terry Gipson, MD	Fifteen people were listed to speak during the public comment period. Due to the committee running early, public comment was taken in two time periods. Public comment was received from the following: • Richard Ensign, PharmD – Pfizer, Second Generation Antihistamines • Dr. David Armstrong – Schering; Second Generation Antihistamines • Jeff Townsend – TAP Pharmaceutical; PPI • Dr. Fran Treadway – Astra Zeneca; PPI
CLINICAL DATA REVIEW • **Second Generation Anti-depressants**	Mark Helfand, MD	Dr. Helfand attended via conference call and presented the RTI-UNC Evidence-Based Practice Center's report comparing the second generation anti-depressants drug class. This report was finalized in October of 2004. The Committee accessed and reviewed a copy of the report prior to the meeting.
CLINICAL DATA REVIEW • **Triptans**	Mark Helfand, MD	Dr. Helfand attended via conference call and presented the Oregon Evidence-Based Practice Center's report comparing the triptan drug class. This report was updated in September of 2004. The Committee accessed and reviewed a copy of the report prior to the meeting.
PUBLIC COMMENT PERIOD – SESSION TWO	W. Terry Gipson, MD	During the second session public comment was received from the following: • Dr. John Jeppson – Allergist; Second Generation Antihistamines • Dr. Amir Karimzadeh – Forest; Second Generation Anti-depressants

		• Dr. Heyrend – psychiatrist; Second Generation Anti-depressants • Tony Sparks, Family Nurse Practitioner – Pfizer; Second Generation Anti-depressants • Marc Bostick, M.D – Glaxo Smith Kline; Second Generation Anti-depressants • Cheryl Rambo, Family Nurse Practitioner – Glaxo Smith Kline; Second Generation Anti-depressants • Martha Tanner, MD – NAMI; Second Generation Anti-depressants • Justine Alderfer, RPh – Wyeth; Second Generation Anti-depressants • Jennifer Brazaner – Glaxo Smith Kline; Triptans • Richard Ensign, PharmD – Pfizer; Triptans • Dr. James Herrold – Triptans
COMMITTEE RECOMMENDATION FOR SELECTED THERAPEUTIC CLASSES	W. Terry Gipson, MD	<u>Proton Pump Inhibitors</u> The Committee determined that all the agents are equivalent, and there are no changes relative to efficacy due to the updated data. <u>Triptans</u> The Committee determined that all the agents are equivalent, and there are no changes relative to efficacy due to the updated data. <u>Second Generation Anti-histamines</u> The Committee recommended that the Department review the prior authorization process regarding the use of first generations prior to authorizing second generation anti-histamines. The Committee determined that all the drugs in this class are equally effective. <u>Second Generation Anti-depressants</u> The Committee determined that all of the agents were effective, but differences in responses could occur with individual patients and in tolerance of specific adverse reactions. They felt several choices, particularly among the non-SSRI drugs, should be available..
SUPPLEMENTAL REBATE INFORMATION *(CLOSED TO PUBLIC)*	Mary Wheatley, RPh	Mary Wheatley presented supplemental rebate information to the Committee members for their review and discussion. This review and discussion were closed to the public.
COMMITTEE FINAL RECOMMENDATION FOR THERAPEUTIC CLASSES	W. Terry Gipson, MD	<u>Proton Pump Inhibitors</u> The Committee recommends Prilosec OTC®, Nexium® and Prevacid® as preferred agents. All other agents will require prior authorization. <u>Second Generation Anti-histamines</u> There will be no changes to the established therapeutic criteria. The Committee recommends all agents as preferred after the client meets the established therapeutic criteria. <u>Second Generation Anti-depressants</u> The Committee recommends that all agents in this class are preferred agents with some restrictions on brand name. it was recommended that the Drug Utilization Review Board publish information on cost differences in its next newsletter.

		Triptans The Committee recommends Zomig ZMT®, Zomig®, Maxalt MLT®, Maxalt®, Relpax®, and Imitrex® as preferred agents. All other agents will require prior authorization.
ADJOURN COMMITTEE MEETING	W. Terry Gipson, MD	The next classes of agents to be reviewed by the Pharmacy and Therapeutics Committee on January 21, 2005 are: ACE inhibitor update, Atypical antipsychotics, and antiepileptic for mood and pain. Dr. Jeff Edwards has resigned from the committee effective immediately due to personal and professional obligations. Dr Gipson adjourned the meeting.

Pharmacy and Therapeutics Committee
Public Comment
November 19, 2004

Richard Ensign, PharmD - Pfizer

Dr. Ensign: My name is Richard Ensign. I'm a clinical pharmacist representing Pfizer pharmaceuticals talking about antihistamines. I appreciate being able to talk to everyone face to face. I commented once before in the summer and it was a speaker phone so it's nice to see everyone eye to eye.

As far as the data submission I cannot comment on that because I was not in the process on the submission of the data. But I did want to highlight two points on the antihistamine because I think there are significant trials that are excluded uh that were not in the analysis. And I'm not sure why there not in the analysis, because they're published in the literature, through a med search last night and they are one of the first that popped up.

One of the challenges with antihistamine trials is in a community your pollen exposures vary depending weather and other things so over the last 10 years there's been a change on how these things are done. And one of the new standards is the environmental control unit where it's basically a room where patients are locked in. I call it a torture chamber 'cause I have allergies. You walk into the room and a certain amount of antigen is infused into the room. So they can measure the patients response: a real good way to look at the head-to-head studies. So there's a variety of head-to-head studies over the last few years and [unintelligible] in these environmental control unit studies. They're published in the literature they were excluded and I'm not sure why they were excluded. They're not even on the list of excluded references. Uh in the head-to-head study there was two comparing Cetirizine to nLoratadine. And just for the sake of time and brevity, both showed 30-50% reduction in the allergy scores on the Cetirizine compared to the nLoratadine. A third study was published this year comparing Cetirizine to nFexofenadine in patients with seasonal allergic rhinitis and in two out of the three time periods Cetirizine had about a 30% reduction in symptoms compared to nFexofenadine. So just adding on to the head-to-head studies that are available and published in the literature, uh Cetirizine does offer clinical advantages for the Medicaid patients because of the variety of formulation. It's a syrup formulation, a chewable tablet formulation, the [unintelligible] tablet and the D formulation which includes sudaphedrine. So I would just ask that we include all the evidence that is out there including these head-to-head trials and I can't explain why they were not included in the Oregon report.

Committee: [unintelligible]

Mr. Ensign: The main allergy journals Annals of [unintelligible] Allergy and Asthma, Journal of Allergy and Clinical [unintelligible].

Dr. Eide: I believe the absences of those studies was submitted in the public comment period and the EPC did look at that and they could give you the actual reasons those studies were not included. That is in written form and is available.

Mr. Ensign: In the back of the report it wasn't indicated as far as why those, the controlled, and they were large studies they were three, four, [unintelligible] in a controlled unit.

Committee: So those comments are posted on a public site.

Dr. Eide: The comments from Pfizer are

Committee: The comments to Pfizer from the EPC

Dr. Eide: Are not on the public site. Those have to be requested.

David Armstrong, PhD – Schering

Dr. Armstrong: I'm Dr David Armstrong with Schering [unintelligible] in the global medical affairs division. I just wanted to start of with asking a question. Do you know what the difference between Benadryl and Sominex is? The label.

The national task force for allergic disorders recommends non-sedating antihistamines be used as first line therapy for allergic rhinitis and chronic [unintelligible]. Thirty-two states have laws regulating the use of certain medications that impact and impair driving ability. And the state of Idaho happens to be one of those states.

I'm here to talk about Clarinex. Clarinex is a long sedating, selective antihistamine. It is the active metabolite of Claritin (Loratadine), but it's different from Loratadine in a number of key ways. Number one it has a longer half-life, it's a 27 hour half-life, versus roughly a 12 hour half-life for Loratadine. It is indicated for seasonal allergic rhinitis, chronic idiopathic urticaria, perennial allergic rhinitis. For those you how treated allergic rhinitis, you'll know that perennial allergic rhinitis and chronic idiopathic urticaria are typically the most difficult to treat. perennial allergic rhinitis because it is more associated with congestion compared to seasonal allergic rhinitis. Claritin is only indicated for seasonal allergic rhinitis and chronic idiopathic urticaria whereas Desloratadine or Clarinex was able to achieve that indication right out of the box. One of the reasons is because of the impact that it has on congestion. In the environmental control chamber Desloratadine has been able to show significant improvements in congestion not only in terms of self reports which are important particularly when talking about cognitive impairment, but from objective measures as well using interior rhinonometry as well as peak nasal respiratory flow. These are claims that other of these second generations antihistamines cannot make.

Importantly [unintelligible] head to head studies, we have one head to head study that was conducted by MedPoint, not by [unintelligible] that looked at persons that failed off of Loratadine (one minute) in that head to head study persons who failed off of Loratadine were statistically show statistically superiority for Desloratadine versus placebo and equivalence to Azelastine which I believe was mentioned earlier as well. Clarinex is not affected by food, does not have any indications with regard to antacid use unlike Allegra, and unlike Zyrtec does not have a warning regarding operation of machinery or driving while using it. I'd also like to say that we just received an indication from the FDA for Clarinex to be used from six months of age, so we have the same pediatric indication as Zyrtec and we are coming out with the syrup formulation at the beginning of January. With that said I'd be happy to take any questions

Committee Can you go back to what you said at the very beginning about the American Academy of allergists…

Dr. Armstrong Both the Academy of Allergy and Immunology and the American College of Immunology recommend non-sedating antihistamines as first line and with respect to the prior auth process that's currently in place it aught to be reversed. You should have a prior auth for first generation antihistamines not second generation.

Committee: So is that guideline in a published consensus.

Dr. Armstrong Yes it is. The allergy report and guidelines by [unintelligible] as well. Those came out about 2001.

Committee: The head to head trial, that was included in the data.

Dr. Armstrong I'm not sure it was. I'm not sure that it was. It came to our attention later on, it was a study published in 2003, published in Jackie by Burger, Bill Burger and again showed that Clarinex was superior to placebo among Claritin failures and clinically equal to Astelin.

Jeff Townsend – TAP Pharmaceutical

Mr. Townsend: I work for TAP pharmaceuticals. I've had the privilege of detailing Prevacid for the last nine years in southeast Idaho doctors, mid-levels and pharmacists. And listening to the recommendations that came up here earlier it sounded there was no new information that came to the table to change the original report which I assume was when the class was originally reviewed is that correct (correct). One thing I would like to highlight, and again I do detail, there is a significant population that deals with Medicaid which is 15 years and younger that would be the pediatric arena. And one thing that Prevacid brings to the table that is significant and different from our competitors is that we have a fast disintegrating tablet and a sachet which is in powder form that can cater specially to this population. It is strawberry flavored so it has a good taste tolerance for children. And then I believe you have the studies and the information that discusses our healing rates [unintelligible] and all the clinical information that you looking at. So I do want to highlight that. And I would entertain any questions you may have.

Committee: Do you guys have an oral suspension?

Mr. Townsend: We have an oral suspension, it's the sachet. It comes in 30 mg and 50 mg. it's mixed with 2 tablespoons of water, again strawberry flavored, it has a bit of a thickening agent in it, and the patient just swallows it down.

Committee: How about a [unintelligible] 'cause the problem with those sachets is it's hard to measure out really small doses.

Mr. Townsend: OK you're talking mg to kg, no we do not have anything within that arena, currently.

Committee: No but does anyone

Mr. Townsend: No, not to my knowledge to be fair. Of course the fast disintegrating tablet which is our new administration that was launched earlier this year it is able to be put down a 5 ml syringe mixed with water, put down, which has very good applications within the hospital arena when they have patients that have a g-tube down in them or an NG tube and it does not have a sugaring agent so it does not clog the tube.

Dr. Fran Treadway – Astra Zeneca

Dr. Treadway: [end of tape] with Astra Zenica and the data I'm going to talk briefly about is either in the EPC report of April 2004. As a mater of fact, two of the three major studies I'm going to discuss were rated the only two studies rated good as opposed to fair or poor. And the other data has been submitted to Oregon.

I'm going to talk about the healing of erosive esophagitis and I'm going to focus on what I consider to be a subgroup of patients who I think it's been shown will do better on Esomeprazole Magnessium than on the other PPI's. I'm going to discuss data from three trials: two were discussed in the Oregon report they are trials by Rictor and Costel comparing Esomeprazole either Omeprazole or Lansoprazole and a third trial of identical study design by Labenz comparing Esomeprazole to Pantoprazole. All three of these trials had large numbers of patients, thousands, which means the studies were powered sufficiently to show the small overall differences that they showed. All had a primary endpoint of four and eight week esophagitis healing over all grades of esophagitis, but all looked at healing by baseline grade

using the LA scale A-D where D is the most severe esophagitis. The study results of all three trials show small significant more patients healed at eight weeks with Esomeprazole than with the comparator. Over all grades of esophagitis the differences range from about 3.4% to 9 1/2%. However, when the data is broken down by baseline grade of esophagitis a very distinct pattern appears. For grades A and B there's really little or no difference in healing rates between the drugs. For grades C and D the differences are really quite significant. In the Rictor study, 17% more patients were healed at eight weeks with grade C and D esophagitis versus Omeprazole in the Costel study 13% more versus Lansoprazole in the Labenz study, 16% more. This comes down if you want to look at numbers needed to treat between 5 and 7 more patients, between 5 and 7 patients is the number needed to treat. Meaning one more person will be healed on Esomeprazole than to the comparative for every 5 to 7 patients treated.

The patterns very clear. As the grade of esophagitis becomes more sever the advantage of Esomeprazole becomes more clear. And symptom relief is a similar phenomenon, but not broken down by grad of esophagitis we used a measure of symptom relief called sustained relief, seven consecutive days, very hard measure of symptom relief and in all these three studies the Esomeprazole patients achieve sustained relief between and three days sooner than the comparative drug. And again the pattern repeats itself in maintenance studies, studies by Lawrence and Labenz. Particularly in grades C and D patients. But really overall, six month maintenance study shows remain in remission with Esomeprazole (one minute) uhm, that's perfect. I maintain that the clinical relevance of this subgroup is first of all it's not a small group [unintelligible] did a study that showed they represent about 25% of the erosive GERD population, they tend to have the more serious consequences from GERD: strictures, ulceration and hemorrhage. They relapse fast, but most importantly they cannot be identified before hand. You cannot identify them except by endoscopy, and not even them because by the time you get to be scoped you have generally been on a PPI for 8 weeks. So I am suggesting that this is a small but important subgroup. They cannot be selected out before hand for specially therapy, but that in fact they benefit from Esomeprazole more than other PPI's to a substantial degree.

Committee: Why do the studies compare Omeprazole or Prilosec 20 mg to Nexium 40?

Dr. Treadway: For a number a reasons. First of all the FDA says you compare indicator dosages. 20 mg is the Omeprazole indicated dosage for healing of esophagitis, 40 mg is the Esomeprazole indicated dosage. So we kind of had to. Really, and there's been studies comparing 20 and 40 of Prilosec of Omeprazole and the studies did not show that 40 heals any more people than 20 in terms of a large healing study. So we did not see that there would be any advantage to that, plus we had to use the indicated dosages. We have acid control data and we some clinical data comparing 20 mg to 20 mg; 20 of Nexium to 20 of Prilosec in a study by Currilus that shows advantage of 20 mg Nexium over 20 mg Prilosec. So we have surrounding data, but no we have not done that.

John Jeppson, M.D. – Allergist

Dr. Jeppson: I don't' think I've said anything in four minutes. First off, how many of you here have allergies? It's about 20 % of the population have allergies, and if you have allergies you know that it can severely effect how you function and what you do from day to day. In fact in quality of life studies, people with perennial allergic rhinitis have a greater impairment in their quality of life than do even asthmatics. So it is a significant disease. Rightly or wrongly the patients I see and if you look at large studies across the US the preferred medication the patients like to take to control the symptoms are the second generation antihistamines. And because of that we rely on the fairly heavily as we treat patients and we faced a real difficult time over the last few years as that availability has been restricted to many of our patients. So my comments today are in support of continuing to provide those to our Medicaid patients. There are just a couple of issues that I'd like to comment on the literature review. I only had a few minutes to look at that last night but there are approximately 1,000 articles reviewed for that literature review. Over 90% were excluded without comment on what they contain. And additional 60% were excluded

because they were of poor quality or because they were on medications that were no longer on the market. And because of that, the articles that were not reviewed left out some important data. So the first question whether or not second generation antihistamines are more efficacious than first generation. It's clear in the literature there's not a huge difference between first and second generation antihistamines as far as how effective they are, so I agree with the conclusions of the summary there. The second question as to whether or not there's a different in the side effects and the adverse events. I think that was very soft played in the presentation, it's clear in the medical literature that has been done with the current second generation antihistamines and also those that are no longer on the market when they are compared head to head versus the first generation antihistamines there is clearly a superiority as far as side effects is concerned. In documenting that, there's two points I'd like to make. First off the State of Idaho and Medicaid recognized over the last two years that that's true because they approved their use in patients that are attending school. It's clear that patients that take the first generation antihistamines have an impairment in their ability to learn and function in school whereas those with second generation antihistamines do not. So that's one case. The second case is the fact that first generation antihistamines it's illegal to take those and to drive a motor vehicle or fly a plane. So it's clear, regardless of what that summary says, there is a huge difference in side effects comparing first and second generation antihistamines. The third question is are there special groups where [unintelligible] may be different? In my opinion I've mentioned them, one kids are in school trying to learn and the second a person who needs to function, driving a motor vehicle and so forth where that impairment could be life threatening. So in conclusion I would encourage those who are making these decisions to continue to provide coverage for the second generation antihistamines so we can provide the best care that we can for our patients. I'm here representing myself and the several hundred Medicaid patients that I care for.

Dr. Helfand: Well I could say a couple of things. First of all the main comment that he made about the excluded studies, and second he focused on the comparison of firs and second generation antihistamines. The excluded studies, I just object to him saying without comment because appendix C lists studies that were poor quality or were compared to medications that were no longer on the market. Out of that 1,000 citations that the search revealed hundreds of those can be liters to the editor, opinions, it's a broad search, so that number of 1,000 really includes lots and lots of material that has no data. Or articles that just talks about antihistamines in general and how they work. So I don't think that the number of 1,000 with 90% exclude is really not that pertinent. Once we get to the ones that are about the subject that we're looking for that's when people should start looking down the list, Appendix C, and tell us specifically are there trials that we called poor quality that they think we mis-rated, or are there trials that compared the marketed drug to one never or no longer on the market that had important information we missed. On the other point, which Susan Carson is here and I'm just gonna refer the question to her, but the other point is how did second generations compare to first generation. Before saying more about that I want to say the main part of our report is to compare the second generation to one another. That's really the focus of the report. I think I missed it, but I wasn't exactly sure what statement in the report the speaker was referring to. Was it the summary of evidence, was there something in there, I'm not sure where it was but the point is the summary of evidence which appears in page 18 and 19 of the report, the key question really are do second generations different from one another in effectiveness. And do they differ from one another in safety and efficacy. And the comparison to the first generation while there is commentary in there about that; it was not the main focus of the report. Do you have anything to add to that?

Yes I would like to make just a couple comments. In comparing second generation antihistamines to each other there were numerous head to head trials that were not included in the data that's presented. And you may have excluded them because you didn't think they were quality studies, but in the immunology field the experts in the field many of them are considered quality papers. And that's what we base our decisions on. And in those it's clear that at least two of the current prescription antihistamines, Zyrtec and Allegra, are clearly superior to Claritin in head to head, well controlled, placebo and blinded studies. I should have commented

on that but in four minutes it's hard to get it all out. And I have 100's of articles in my person file that if we had the time I could pull them all out to present some additional data that supports what I've been talking about.

All of the reports have a public comment period where the report is placed on our website and anyone can suggest to us information we may have missed or flaws in our interpretation of the data. And of course we did get comments of that kind. If there are two specific studies you want to bring up, page 95 of the full report is where the list of poor quality trials, trials we decided were poor quality trials. I'll tell you we are not trying to [unintelligible]. If there is disagreement about the quality of the study, the best thing for us is to look at it again and decide why it may not be poor. We're certainly open to that but we need the specific references whether it was listed here, and if not what studies you're talking about.

Dr. Amir Karimzadeh – Forest

Dr. Karimzadeh: I'm here to show the advantages, the therapeutic advantages of Lexapro over other antidepressants. There has been data presented to Evidence Based of Oregon. I want to start out by saying as everyone has heard already that Escitalopram is the [unintelligible] to Citalopram, however the biological activity and the therapeutic benefits of Citalopram reside exclusively in Escitalopram. Escitalopram is the most selective SSRI today. It is the most selective SSRI in its class and it has virtually no affinity for other neurotransmitters. Hence it's excellent tolerability. Now the efficacy of Escitalopram in the treatment of depression has been demonstrated in multiple clinical trials. Those would be some of the pivotal trials such as the US fixed dose study in outpatients and that was [unintelligible] trial as well as the European fixed dose study which was authored by Dr. Wade. There's also a head to head study, pooled analysis, by Dr. [unintelligible] that compares Lexapro versus Citalopram. Sustained improvement of systems have been shown as early as week one or two meaning that your patients come in and report that they are getting better as early as week one or two which we were never able to prove with Citalopram, and I haven't seen it with other antidepressants as well. Continuing improvement and effective prevention of relapse has been shown in a long term study and that 36-week study [unintelligible]. Escitalopram has also been proven effective in general anxiety disorder. I noticed earlier today there are two agents approved for GAD as far as SSRI goes Citalopram and Escitalopram is the other agent that has the GAD indication. We have also filed and SNDA for panic as well as an SNDA for social anxiety disorder. Escitalopram is safe and very well tolerated, that's been shown in the clinical trials as well as naturalistic settings. In the clinical trial Escitalopram discontinuation due to adverse events was 6% versus 16% with Citalopram. I'm going to jump to the end, I just want to mention that Lexapro is just as good or better than any other antidepressant, so we have that as far side effect profile goes. Its [unintelligible] is negligible, its protein binding is only 56% therefore you have a significantly reduced drug to drug interaction. And its dosing, when you talk about dosing it has a very narrow dosing range, 10-20 mg. All those three things add up to a better compliance with patients and as a result you have a better therapeutic outcome.

Dr. Heyrend, Psychiatrist – Pfizer

Dr. Heyrend: I'm here to make some clinical observations rather than to present a paper, and very very simply over the past 15 years I've averaged about 15 teenagers in the hospital and

Dr. Gipson Excuse me Dr. Heyrend, you need to identify if you are speaking of your own volition or you are here at the request of

Dr. Heyrend I'm here of my own volition. And so consequently the average length of stay is 105 days. I will admit that very few of these kids is from Idaho, only about 9%. But what's happened is that in taking care of these kids and the other 25 or 30 that I also supervise we've found that of the SSRI's if you use first line, we put two on the list, we put Zoloft and we put Lexapro and those

are the two that we've had the least amount of difficulty. And my advantage of course is I have the kids long enough with an average stay of 105 days that if there are going to be complications I see them. So that's what I wanted to point out. And the other observation was that I understand that as a generic Prozac is extremely inexpensive and often very, very efficacious. However, I have not had as good an experience with smaller children, 12, 12 to 15 as I have with the other two. I just wanted to give you this information. I feel it was very important.

Tony Sparks, Family Nurse Practitioner – Pfizer

Ms. Sparks: I'm Tony Sparks. I'm a Family Nurse Practitioner and I represent myself and the Medicaid patients that I take care of in the field of psychiatry. First and foremost, I hope that you look as all of these antidepressants as a safety. It's not just in psychiatry that we see them. They're used in OB/GYN, internists. Nobody comes in with just depression. There's no such thing as just depression. They have sleep disturbance, anxiety, they have OCD, they have PTSD, they have though disorders. So we use these broad medicines hopefully to cover a number of those areas so we don't have to use a medicine for every symptom they have. One of the biggest issues is compliance. When case managers, when families bring me in bags of medicines they don't want to take because of side effects or it's not effective for them, I never get stimulants back, I rarely get a benzodiazepine, next thing I get is antidepressants. First it's tricyclic's then I get the other medicines back., but it's not many of them, because they take those medicines [unintelligible] bags of them. They're safe medicines, they're good medicines. Zoloft is very well tolerated in kids and adolescents, but especially the elderly and geriatrics which I haven't heard a lot about in these studies. It's well tolerated, they take their medicines and they feel better on it. And that's from a clinical standpoint, seeing real people and not just the studies. Thank you.

Marc Bostick, M.D – GlaxoSmithKline

Dr. Bostick: I was invited to speak by Norm. I'm not being paid for it, I'm not even getting a pen. So what I've come up here to talk about is just with Wellbutrin XL versus Bupropion SR, and ordinary Bupropion. I'm doing this for free, because I do feel pretty strongly and I think it's common sense that anything you can take just once a day is actually going to be utilized and used and be helful far more than if you have to take it twice or three times a day. As a doctor and this happens every day, we have this little dance with our patients, I ask them how they are doing, they tell me their taking their medicine, and I pretend to believe them. But in reality all patients across the board [unintelligible] miserable in a way, miserable [unintelligible] and people with depression even more so than in the general medical conditions. And I think we can even say with Medicaid patients probably, I don't have the numbers to add this up, but I think Medicaid patients are even less reliable than the people with good life functioning [unintelligible]. So we're talking the population most vulnerable to medication non-compliance and were trying to give them the medication that they are having to take 2 and 3 times a day, I just think they are not going to do as well. In my clinical experience that is born out in patients across the board. You start them out on Wellbutrin XL people come back saying I feel better and it's because your taking it knucklehead. With cost you guys probably know more about cost than all other [unintelligible] but medication that you don't take properly in illness is as dangerous and as debilitating as depression can cost a lot if you don't get good efficacy, both in [unintelligible] potentially suicides.

Cheryl Rambo, Family Nurse Practitioner – GlaxoSmithKline

Ms. Rambo: In my Medicaid population I've been asked to speak for Paxil CR. I'm just going to tell you about what I see. In using Paxil [unintelligible] side effects when I started switching to Paxil CR for depression and social anxiety disorder and panic disorder I noticed a greater increase in compliance with my patients, less sexual side effects, [unintelligible] positive because people continue to take the medication. Really improved compliance and in social anxiety disorder I

didn't have to use benzodiazepines which is the other [unintelligible] great not to have to use multiple medicines for each individual problem a patient has. And I find Paxil [unintelligible] is a superior product. I hope that you will consider putting it on the formulary because I think the Medicaid population deserves to have this choice. Thank you.

Martha Tanner, MD – NAMI

Dr. Tanner: I'm a physician retired. I worked at Eastern Idaho Regional Medical Center for 23 years as an internist and as an infectious disease specialist. Did a lot of work with formulary and hospitals. We save a lot of money with antibiotics. I'm here, not representing the drug companies at all. I'm here representing NAMI, National Alliance for Mentally Ill because I have a son with very severe schizophrenia. And boy have I been introduced into the system. And I appreciate very much the psychiatrists who have taken very good care of him. But what I have learned in this role as a family member and working with many families in NAMI is that people do not respond to psychiatric medications like they respond to antibiotics. And you can't predict necessarily ahead of time who's going to respond to what drug. And I think what NAMI would abhor most of all a formulary that restricted the drugs. A particular one that would force a person who has been stable on a particular antidepressant to be changed another one arbitrarily. And I'd like to give you two articles which I think address this issue. This particular article in the American Journal of Managed Care, I believe it's 1999 showing that they had more dropouts in their patients from a formulary that restricted the choice of antidepressants to one drug than a formulary that restricted it to two drugs. And I think it's exactly as Dr. Helfand pointed out in his studies, that 40% of patients don't respond to the initial antidepressant. And a lot of times it's because they have [unintelligible] or an individual adverse reaction that means that their doctor needs to change their medication to something they will take. Because if they don't take it they will not respond. The other article I'd like to submit is from Psychiatric Services from 2003. And this is strategies. Now I've learned a lot about strategies in dealing with saving money with antibiotics. And there are very good things you can do that do not require a restricted formulary. I never restricted an antibiotic in a formulary until the last few months of my practice. It's much easier to implement a formulary where you educate doctors, you explain the relative cost of drugs. And doctors respond quite well to that type of education. In this article they proved they were able to save about $700,000 in their managed care situation. Just with this system of informing doctors and getting back to them on a regular basis. And I'd like to submit this article which demonstrates they were able to really change their physicians use of drugs based on this information.

Justine Alderfer, RPh – Wyeth

Ms. Alderfer: I want to first thank you all for letting me speak today. My name is Justine Alderfer. I am a pharmacist. I work in the medical group at Wyeth Pharmaceuticals. And I'm here to give you a brief over view of Venalfaxine. Venalfaxine's actually the first serotonin norepinephrine reuptake inhibitor available in the US. It's been available for approximately 10 years. It's been prescribed in up to about 10 million patients thus far. The XR formulation has been approved for major depressive disorder, generalized anxiety disorder and also socialized anxiety disorder. We have excellent data with regard to relapse of patients with depression in studies that have gone up to six months and also 12 months duration in length. Basically, well historically, people have thought that antidepressants are equally efficacious in all patients. I would propose that new evidence suggests that patients do respond differently to antidepressants with different mechanisms of action such as SSRI versus SNRI like Venalfaxine. There have been several pooled analyses and meta analyses that have compared remission rates. Venalfaxine to SSRI's. and keep in mind today remission is actually considered to be the gold standard of treatment where we want our patients to get to. And there's a pooled analysis that pooled about 16 trials in which Venalfaxine is compared to SSRI's. there's also been two meta analysis; one with 8 trials and also one with 32 trials that also compared remission of Venalfaxine to SSRI's. The

SSRI's included and Fluoxetine, Fluvoxamine, Sertraline, Paroxetine and also Citalopram. And in all three of these meta analysis and pooled analysis the remission rates for Venalfaxine were significantly greater than for those for SSRI's. Now keep in mind the studies were about 6-8 weeks duration in length they did not exclude patients who had previously failed at SSRI's and although there were various comparators Fluoxetine was the most commonly used in these trials. Now I mentioned the study that had 32 pooled studies involved, we also looked at relief of semantic symptoms for depression for Effexor versus SSRI's. Basically we really care about the other symptoms like fatigue, aches and pains that patients have along with depression and once again Venalfaxine [unintelligible] greater with regards to relief of these semantic symptoms versus SSRI's. With regard to metabolism, Venalfaxine metabolite to an active metabolate [unintelligible] Venalfaxine. It does not have a strong inhibition or [unintelligible] and with regard to dosing, the XR formulation is once daily with the initial starting dose at 75 mg, although patients can start at 37.5 mg. The [unintelligible] is normally 75 to 225 mg per day. And basically just to summarize what I just told you, the key points I wanted to hit on is that Venalfaxine has multiple [unintelligible] as I mentioned to you. It does have once daily for the XR formulation. We have excellent data with regards to remission rates in patients as compared to the SSRI's. And lastly, our drug interaction profile is fairly good. I think I didn't mention that our protein binding is pretty good, it's less than 30%. I just wanted to summarize those are the key points I wanted to hit on with Venalfaxine. And I wanted to thank you all again for your time.

Jennifer Brazaner – GlaxoSmithKline

Ms. Brazaner: I thank you for the opportunity to speak with you about the importance of maintaining Imitrex's status on the Idaho PDL. My name is Jennifer Brazaner, I'm a regional medical scientist with GlaxoSmithKline. We just finished this project, process in Oregon, Washington Michigan and Alaska. Let me share with you why they all chose to keep Imitrex on their PDL. Worldwide, Imitrex is the gold standard among triptans and is the market leader. We are the most widely studied triptan on the market and therefore possess a vast library of safety and efficacy data. Imitrex is available in three formulations. Each offering unique differences in onset and efficacy. The onset of pain relief with Imitrex inject is 10 minutes, 15 minutes with the nasal spray and we are pleased of announce the onset efficacy with Imitrex 100 mg reformulated tablets is now 20 minutes. We are the first oral triptan to surpass the 30 minute onset point. Because of the multiple formulations offered by Imitrex patients have the ability to rescue if necessary. This means patients may use Imitrex inject along with Imitrex tablet or nasal spray in the same 24 hour period. Application of this treatment strategy is unique to Imitrex because utilization of two different triptans in the same 24 hour time period is contra indicated. For instance Imitrex injection and a different tablet. Additionally, since we know that 30-40% of migraineers report that nausea and vomiting interfere with their ability to take ability to take tablets, Imitrex injection and nasal spray offers them an alternative by bypassing the GI tract. It's important to note that marketed melt formulations do not do this. In January 2004 Imitrex was reformulated to a rapid release tablet. Why did we do this? We know that gastric stasis occurs during a migraine significantly decreasing absorption and dissolution of a tablet. The reformulation Imitrex tablet was designed to dissolve irregardless of the presence of gastric stasis. Studies have shown nearly 100% of the reformulated tablet dissolves in 10 minutes compared to less than 10% of old formulation. So we know it dissolves faster. Studies then showed that time to maximum concentration occurred 10-15 minutes earlier with the reformulated table. So not only does it dissolve faster, it gets absorbed into the bloodstream faster. Finally, studies have shown that pain free rates, 2 hour pain free rates with reformulated Imitrex 100 mg tablets are 75%. Patients that took Imitrex early in migraine achieved pain free at 2 hours in 75% of patients. Comparing the triptans obviously involves sifting through a large amount of data I just want to point out a few things to you. No triptan has proven superior to Imitrex in adequately designed and well controlled trial. Several head to head trials have used over encapsulated Imitrex. While aware to the decreased efficacy due to over encapsulation and although the OHSU triptan report excluded studies of poor design, it did use the [unintelligible]

meta analysis which did include over encapsulated Imitrex data. No triptan has compared itself to the reformulated Imitrex tablet, and none of the information on the Imitrex table is included in the OHSU report. The [unintelligible] registry for Imitrex has richest database of [unintelligible] exposure in the market. This is important because we know migrates affects women during their childbearing years. Imitrex has minimal drug interaction not the [unintelligible] therefore it does not further affect the clinical decision making process. In closing the clinical experience and multiple formulations of Imitrex offer the flexibility to utilize a stratified approach with proven efficacy and safety. Thank you.

Richard Ensign, PharmD – Pfizer

Dr. Ensign: I wanted to say just a few things on the triptans. Luckily this time the data is in the review. A couple of things I'd like to draw your attention to. Page 15-16 of the review it looks at the primary endpoint of 2 hour headache response. Dr. Edwards pointed out there's a lot of data in this review however if you take a step back and look at these trials, the primary endpoint from the majority of these trials is headache response at 2 hours. There's not a secondary [unintelligible] endpoints and in the summary any time there's a difference [unintelligible]. But it's important to take a step back and just look at that primary endpoint of the 2 hour headache response. 'cause there's only a couple of studies that have really shown a difference in the triptans that are on the market. The ones that have are eletriptan versus sumatriptan, eletriptan versus naratriptan, and also the rizatriptan versus naratriptan, although rizatripatn was not different than sumatripan at that 2 hour headache response. In the eletriptan versus sumatriptan not only did it achieve clinical improvement at the 2 hour response it continued at many other endpoints of the study such as 1 hour pain relief, 2 hour pain free, patient satisfaction, return to normal function, escape medication, and nausea phobia, and other symptoms. I guess my plea to you would be for you to not exclude this study as was done from the summary on the basis of encapsulation. 'cause if you look at the data the studies that were done on that encapsulation formulation, I can't speak for all encapsulation formulations but at least on the sumatriptan/ eletriptan studies, it met the FDA requirements for not only AUC/CMAC, all the FDA characteristics for being [unintelligible] but also there [unintelligible] label studies done where you could actually measure in humans how that tablet dissolved. And surprisingly they actually found in the human studies the encapsulated sumatriptan complete disintegration was at 16 minutes compared to non-encapsulated which was 18 minutes. So the encapsulated dissolved 2 minutes sooner than the non- encapsulated. So the other way of looking at that, it's very difficult in these studies to head to head compare different studies with different patient populations. So one of the things that's done in the literature is subtracting out the placebo response. Instead of just looking at what the response was in the different studies, but most of these that are placebo controlled, subtract that out. If you look at what they call therapeutic gain where you subtract out placebo response, the encapsulated [unintelligible] triptan falls out right in the middle of the rest of the sumatriptan arms. So I just urge you not to dismiss that because it was a proven scientific method shown to actively blind these studies and all the kinetic studies shown to be therapeutically equivalent. Any questions.

Dr. James Herrold – Pfizer

Dr. Herrold: I was asked by Ortho McNeil and Pfizer to present some of my thoughts on some of their respective drugs in due time as I have a 2:30 patient. Before I go into, I'm not going to try and present a lot of data here but I would just advocate that we do keep triptans on the formulary because I do see tons and tons of migraine patients and I'd much prefer prescribing triptans as Vicodin. There's a huge problem with drug abuse across all patients and the triptans do allows us to sort out how truly does have migragrain pain as apposed to drug seeking. So I would encourage the board to make as many triptans as possible available including all five of the short acting ones. I think the data is really hard to sort through and you guys have your work cut out for you in trying to find out what is the best triptan. The second thing I'd like to say is

the placebo response in all headache treatments is really high it's 30%. These trials are just fraught with subjectivity. And also you need to look at headache relief at 2 hours versus headache pain free. So somebody can get just improvement in their headache that's different than headache free. And then with regards to the meta analysis, certainly there's statistical problems with meta analysis. There were I believe 25,000 patients taking some sort of triptan during those studies. All the drug companies submitted data, they were all given that information after it was sorted through, before it went into the paper and they were all given their chance to make their comments as to the validity of it. And there's, I'd just advocate that you look at the meta analysis see which drugs were best tolerated which were most efficacious. Another point I'd like to make or request, if patients use more than the allocated 6 or 9 triptans each month that you consider overriding that number if the patient is on prophylactic medication and under a physicians care who's actively trying to treat the patient. 'cause not everyone gets by on 6 triptans a month, and it's hard to treat them, even if they're on 3 prophylactic medication and they get 6 triptans and they use 2 pills per headache. They're allowed 3 headaches per month and anything over that it's too bad here's your Vicodin, or go to the ER. So I would just encourage you to cipher through the data, read it with a grain of salt and the meta analysis does have validity. I've been to conferences sponsored by various triptan companies. The headache guru's do put some faith in it because of the statistical power of 25, 000 patients. And they weren't double blinded, placebo controlled studies, they weren't open label trials. And so, in summary I would just really encourage you guys to keep triptans on the formulary, and if it's doable, keep all five of the short acting triptans, not necessarily Amerge or Frova but the short acting ones. In my experience they've been the most efficacious for the patient. Any questions?

Committee: Jim, you mentioned about the pain response versus being pain free. Is one of those measures more important?

Dr. Herrold: Pain free is much more object. My headache versus my headache when from a ten to a five. Because, the idea is there's so much subjectivity, you have patients that have different pain tolerances. So somebody's 10 out of 10 headache is a 5 out of 10 for another. So for it to be objective I think pain free is what the studies are migrating to and you'll see more current literature look at pain free at 2 hours. So when you look at that data keep in mind the subjectivity of people's pain.

Committee: When you look at the onset of action, how do you determine that, is that pretty important?

Dr. Herrold: the pharmaceutical companies make a big deal of that. Quite honestly in practice I give patients 2 or 3 different triptans, and they pick their favorite one, they don't read the studies they just come back and tell me what works. I think we stress the importance of taking the drugs early and I think there's some importance of getting the drugs into the system quicker. But I've more than one national headache expert say that the triptans, the triptan companies are going to hate me for saying this but triptans are more alike than they are different, so you need to look at cost efficacy and that's why I'd almost say I don't know if these drugs will be over prescribed or more prescribe if all 5 were available. I think it's very difficult for any person to look at this data and make sense of it, so ultimately it will depend on the cost of these medications.