Pharmacy and Therapeutics Committee Meeting Record

Date: 9/16/05 **Time:** 9:00 a.m. – 5:15151515 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; Mic Markuson, RPh.; Phil Petersen, M.D.; Richard Pines, D.O.; Rick Sutton, RPh; Stan Eisele, M.D.; Tami Eide, PharmD

Committee Members Absent: Stephen Montamat, M.D.; Thomas Rau, M.D.

Committee Members Absent: Mic Markuson, RPh.; Catherine Gundlach, PharmD

Agenda Item	Presenter	Outcome/Action
CALL TO ORDER	W. Terry Gipson, MD	
• **Roll Call**	Linda Edson	Ms. Edson called the roll. One voting and one non-voting member were not present.
• **Reading of Confidentiality Statement**	W. Terry Gipson, MD	The confidentiality statement was read by Dr. Gipson.
• **Approval of Minutes from March 18, 2005 Meeting**		The minutes from the May 13 2005, Committee meeting was approved with one clarification note regarding approved dementia.
• **Discussion of Key Questions for Upcoming EPC Drug Effectiveness Review Studies**	Tami Eide, PharmD, BCPS, FASHP	The draft key questions for statins, second generation antidepressants, drugs for Alzheimer's disease, TZD agents were discussed.
DUR PROPOSED PRESENTATION • **Calcium Channel Blockers**	Heather Brandt, PharmD	Dr. Brandt presented a review of calcium channel blocker outcomes conducted after the prior authorization implementation of this drug class in July of 2004. The purpose of this review was to obtain information regarding CCB utilization. The results of this outcome study indicate that the majority of claims are for amlodipine, diltiazem, and verapamil. Most switches in therapy were between these agents. There were more office visits in the verapamil group.
DUR PRESENTATION • **Long Acting Opioids**	Chris Owens, PharmD	Dr. Owens presented a review of long acting opioids conducted on opioid claims data for the period of January 2004 through April 2005. The purpose of this review was to obtain information regarding the clinical and financial outcomes resulting from the prior authorization of this drug class. Overall, the results of this outcomes review indicate that most patients were switched to preferred agents without negative consequences, clinically or financially.
PUBLIC COMMENT PERIOD	W. Terry Gipson, MD	Six people were listed to speak during the public comment period. Public comment was received from the following: • Dr. Robert Lee – Calcium Channel Blockers

		• Darren Hill, Pfizer – Calcium Channel Blockers • Dr. Chad Wolf, Boehringer Ingelheim – Antiplatelet (Aggrenox) • Dr. Ann Speiser, OMP – LAOs • Dr. Richard DeBose, Director of the Idaho Pain Clinic – LAOs • Dr. Robert Lee – Antiplatelet • Mark Haumschild, Sanofi-Aventis – Antiplatelet (Plavix)
DRUG CLASS REVIEW • **Newer Antiplatelet Drugs**	Selma Gearhardt, PharmD	Dr. Gearhardt presented a review of Newer Antiplatelet drugs including indications, how the drugs work, the drug-drug interactions, availability, and dosing. This review included the following drugs: • Ticlopidine (Ticlid®) • Clopidogrel (Plavix®) • Aspirin/Extended-release Dipyridamole (Aggrenox®)
CLINICAL DATA REVIEW • **Newer Antiplatelet Drugs**	Janet Dailey, PharmD	Dr. Dailey attended via conference call and presented the Southern California Evidence-Based Practice Center's report comparing the newer antiplatelet drug class. This report was finalized in June of 2005. The Committee accessed and reviewed a copy of the report prior to the meeting.
CLINICAL DATA REVIEW • **Long Acting Opioids**	Roger Chou, M.D.	Dr. Chou attended via conference call and presented the Oregon Evidence-Based Practice Center's updated report comparing the long acting opioid drug class. This report was finalized in April of 2005. The Committee accessed and reviewed a copy of the report prior to the meeting.
CLINICAL DATA REVIEW • **Skeletal Muscle Relaxants**	Roger Chou, M.D.	Dr. Chou attended via conference call and presented the Oregon Evidence-Based Practice Center's report comparing the skeletal muscle relaxant drug class. This report was finalized in May of 2005. The Committee accessed and reviewed a copy of the report prior to the meeting.
CLINICAL DATA REVIEW • **Calcium Channel Blockers**	Kim Peterson, MS	Ms. Peterson attended via conference call and presented the Oregon Evidence-Based Practice Center's report comparing the calcium channel blockers drug class. This report was finalized in March of 2005. The Committee accessed and reviewed a copy of the report prior to the meeting.
DUR PRESENTATION • **Skeletal Muscle Relaxants**	Chris Owens, PharmD	Dr. Owens presented a review of the skeletal muscle relaxant drug class. The purpose of the presentation was to characterize the utilization of SMRs in the Idaho Medicaid population since the P&T committee's review of the class and to assess the impact of recent educational materials on the prescribing and dispensing patterns of SMRs. The results indicated that following Idaho DUR educational mailings in July and August 2004, utilization of carisoprodol decreased only slightly.
MEDICAID MODERNIZATION ACT	Randy May, Medicaid Deputy Administrator Tami Eide, PharmD, BCPS, FASHP	Mr. May and Dr. Eide presented a report to the Committee regarding the Medicaid Modernization Act. The report highlighted what the MMA consists of, and how the MMA will impact Medicaid, current Medicaid participants and future Medicaid participants, as well as Medicare participants.

COMMITTEE DISCUSSION AND CLINICAL CONCLUSIONS FOR SELECTED THERAPEUTIC CLASSES	W. Terry Gipson, MD	Newer Antiplatelets Based on the evidence that was presented, the Committee consensus was that overall there is no evidence that any of these drugs are more efficacious than another. Although the committee concluded that there are some safety issues with ticlodipine, it has a definite place in therapy and should remain available. Long Acting Opioids Based on the evidence that was presented, the Committee consensus was that there is no evidence that any of these drugs are more efficacious than another nor does any agent provide any safety advantage over any other. Skeletal Muscle Relaxants Committee consensus was that there is no evidence that any of these drugs are more efficacious than another. Based on the clinical evidence, Drug Utilization Review Board report, and the recommendation of the Idaho Board of Pharmacy the committee is very concerned about the safety and potential abuse of carisoprodol (Soma®) in the Idaho Medicaid population. Calcium Channel Blockers Based on the evidence that was presented, the Committee consensus was that there is no evidence that any of these drugs are more efficacious than another, nor do any provide any significant safety advantages.
PUBLIC MEETING ADJOURNED	W. Terry Gipson, MD	The next classes of agents to be reviewed by the Pharmacy and Therapeutics Committee on September 16, 2005 are ADHD, Antidepressants, and Statins. Dr Gipson adjourned the public portion of the meeting.
SUPPLEMENTAL REBATE INFORMATION *(CLOSED TO PUBLIC)*	Randy May, Medicaid Deputy Administrator	Mr. May 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	Newer Antiplatelets The Committee recommended Ticlopidine, Aggrenox, and Plavix be designated as preferred agents. All other agents in the class are to be designated as non-preferred. The Committee also recommended that the Department create diagnosis/drug specific guidelines for duration of use based on best practice standards. Length of use that exceeds these guidelines (maximum 12 months) will require Prior Authorization. Calcium Channel Blockers The Committee recommended no changes to the current preferred drug list and therapeutic criteria. (Currently brand name products with generic equivalents require prior authorization) Long Acting Opioids The Committee recommended the following: • Morphine Sulfate (Extended Release), Methadone and Kadian® be designated as preferred agents. All other agents in this class will be designated as non-preferred and require prior authorization.

		• A required (30 day minimum) trial period and documented failure of a preferred agent before the use of a non-preferred agent will be authorized. • Current prior authorization criteria for Duragesic® to remain in effect. • Patient's with a diagnosis of malignant pain or history of chemotherapy in the past year will be exempt from the prior authorization criteria <u>Skeletal Muscel Relaxants</u> The Committee recommended that carisoprodol (Soma®) and Skelaxin® be designated as non-preferred and require prior authorization. The Committee recommended the following therapeutic criteria for carisoprodol: • Carisoprodol use limited to 34 days or less. • Documented failure of two (2) preferred agents (based on adequate trial of at least one week per agent) will be required before carisoprodol use will be authorized. • Concurrent carisoprodol and opioid use will require prior authorization. • Additional prior authorization requests for carisoprodol, after initial approval, will not be granted for at least six months following the last day of previous therapy. • The committee recommends a thirty (30) day taper period for chronic carisoprodol users.

Pharmacy and Therapeutics Committee
Public Comment
July 15, 2005

Dr. Robert Lee – Calcium Channel Blockers

Dr. Lee: Hello. My name is Dr. Robert Lee. I'm a cardiologist practicing in Boise and I'm representing myself. I'm here to talk to you about my position on the CCB's, specifically Norvasc. Norvasc or amlodapine is as I understand felt to be one of the more expensive calcium channel blockers and I was actually looking at the data the practicing physicians have which is Epocrites. I found out actually that Norvasc 10 mg is less expensive than generic Nifedipine sustained release. So that was kind of interesting to me. Amlodapine has some of the most extensive data available with the calcium channel blockers at this point. There are numerous studies; it's one of the drugs that is used as a comparator that you will see in all your [unintelligible] data. It is used as a comparator against many of the other classes so it used as a comparator against ARB's, ACE's and the other drug categories. One of the studies that I think is very, very important in looking at, that was not addressed in the OHSU stuff is the ASPECT trial, which compared Amlodapine plus an ACE inhibitor but the ACE inhibitor was then added on against beta blocker with an add on of a diuretic. And there was significantly improved outcomes with the use of calcium channel blockers. And some of that was felt to be the fact that the calcium channel blocker Amlodapine drops blood pressure more quickly. The ASPECT trial was planned for a five year trial and stopped two years early by the Safety and Monitoring Committee because of a very statically improvement in outcomes with the combination of the calcium channel blocker and the ACE inhibitor. And then finally I would have to say that Amlodapine is clearly the leader as far as what's prescribed in our community. We as cardiologists, the internists I think lean quite heavily towards Norvasc and Amlodapine vs the other calcium channel blockers. We don't really have to much access to nicardipine, felodipine is really not used a whole heck of a lot and Procardia or Nifedipine generic is really not used as much as possibly is should be, but I think that one of the considerations should be that the vast majority of our patients are going to be taking Amlodapine and if we are charged with changing all these people from Norvasc to generic Nifedipine or some other drug it is going to be just a huge, huge burden. I would support that Amlodapine be continued on the Medicaid formulary. Are there any questions?

Darren Hill, Pfizer – Calcium Channel Blockers

Mr. Hill: My name is Darren Hill. I represent Pfizer. I am in the sales division with Pfizer and just briefly just wanted to share with regards to calcium channel blockers in the antihypertensive class they are a bit unique relative to antihypertensives. When you take a look at ACE inhibitors, ARB's, even diuretics often times they are seen to be interchangeable, but when it comes to the calcium channel blocker class and choices from physicians, overwhelming Norvasc has been the product of choice. I see that on the agenda later on that you are going to be discussing the Medicaid Modernization Act and how that will affect Medicaid and I would venture to guess, although I don't have the data, that many of the patients that you have on Amlodapine or on Norvasc in Medicaid are dually eligible for both Medicare and Medicaid and those dually eligible patients will be automatically enrolled into Medicare and Medicare will begin taking out their prescription drug benefits after January 1, 2006 and so for those patients that are on Norvasc I would ask that you consider the fact that making a change to them may impact their ability to get a medication that physicians have seen as most appropriate for them and would impact their ability to potentially to get that beyond January 1st or they may have to switch and switch back after that time. So I think that the costs involved especially for patients that have [unintelligible] isolated systolic hypertension are typically going to be dually eligible for both Medicare and Medicaid and the cost to the state beyond January 1st will be much less by keeping Norvasc on board so I think that a choice that allows the physician access to Norvasc really will benefit patients that are in Medicaid in the State of Idaho. Thanks.

Dr. Chad Wolf, Boehringer Ingelheim – Antiplatelet (Aggrenox)

Dr. Wolf: Thank you. My name is Dr. Chad Wolf. I'm a medical scientist as Boehringer Ingelheim. I'd like to talk today a little bit about the benefits of using Aggrenox. Aggrenox as you know is a capsule taken twice daily and indicated for the secondary prevention of stroke in patients who have had previous Ischemic stroke or Transient Ischemic attack. Aggrenox is a novel formulation and the capsule contains 25 mgs of aspirin tablet and 200 mgs of Dipyridamole pellets. Each Dipyridamole pellet has an extended release coating and a core of Tutaric acid for increased absorption. In individuals with low gastric acid the extended release Dipyridamole in Aggrenox provides 50% higher bioavailablity than the immediate release Dipyridamole under the trade name Persantine. And I think it is important to mention that Aggrenox has prescribing information that contains a cautionary statement, [unintelligible] by FDA that states, "Aggrenox is not interchangeable with the individual components of aspirin and Persantine tablets." Aggrenox inhibits thrombosis through the combined actions of these two components. The first of which is aspirin which irreversibly inhibits cyclo-oxygenates [unintelligible] decreases the thromboxine [unintelligible] which is a powerful inducer of vasoconstriction. A 25 mg dose inhibits aggregation of platelets by 90% within one hour. The second of which is Dipyridamole which has its affects on both the vessel wall and platelets and [unintelligible] by several factors. It inhibits the uptake of Adenosine resulting in increased local concentration of Adenosine and thereby decreases platelet aggregation; secondly it augments the affects of nitric oxide which in turn increase vasodilation and inhibits platelet aggregation and adhesion to vessel walls. And it also increases inflammatory factors. Like NDP9, and MCP1, both which are markers of Athrogenesis. Both aspirin and extended release Dipyridamole are independently anti-thrombotic and their affects are directly additive. Aggrenox is twice as effective for stroke prevention as aspirin alone. This [unintelligible] anti-thrombotic affect and perhaps the additive benefit of other modes of action of Dipyridamole such as the affects of vessel walls and anti-inflammatory properties as mentioned. Now in the European stroke prevention study 2 trial Aggrenox showed a statistical significant relative risk reduction for stroke by 22% compared to aspirin. Further the difference in efficacy increases in higher risk patients. The secondary input analysis did reveal a 62% relative risk reduction verses placebo that was also significant in other vascular events, including Peripheral Artery Occlusion and Deep Venus Thrombosis although the number of such events in the study was small. Now as you know 50 mg of aspirin per day is accepted and recommended for stroke prevention by the FDA, AHA, ACCP and the NSA. Importantly it has been shown that addition of Dipyridamole to aspirin does not increase bleeding risk. Aggrenox is endorsed as a first line anti platelet agent for the prevention of non cardiac embolic cerebral [unintelligible] events and ACCP 2004 stroke guidelines. Lastly I would like to say the ongoing progress trial being done by Boehringer Ingelheim will enroll 18,500 patients at over 700 sites internationally and is designed to investigate the superiority of Aggrenox verses Plavix in secondary stroke prevention. Thank you.

Dr. Ann Speiser, OMP – LAOs

Dr. Speiser: Good Morning. I'm Dr. Ann Speiser, I'm a scientist with Janssen, Ortho McNeil. I appreciate the opportunity to share some of the recent findings regarding Duragesic. As you know Duragesic is indicated for use in patients with chronic pain that cannot be managed by lesser means and that require continuous opioids administration. It shouldn't be used in the management of acute or post operative pain or in minor or moderate or intermittent pain that can respond to non opioid therapy. And additionally it shouldn't be used, started at doses depleting 25 micrograms per hour due to the potential for life threatening hyperventilation. That out of the way, Duragesic's efficacy in treated chronic pain has been proven in randomized double blind controlled studies as is well accepted in the pain community. Its unique formulation allows it to differ from other long acting opioids. It's the only long acting product that is indicated for both children and adults. It does provide an alternative for patients who cannot swallow medications. It has consistent and dependable pharmacokinetics and it's association with hospital admissions secondary to narcotic use or abuse is low and in fact, the drug abuse warning network studies these things and publishes articles on it and in general and Duragesic in specific remains one of the lowest causes for admission for narcotic abuse into hospital ERs. Especially in comparison to Oxycodone, Hydrocodone and Methadone. These factors, its efficacy and its safety and it's low risk for abuse have all contributed to it being the exclusive long opiate on eleven state PDL's across the country. We have some more recent data that further extends our knowledge of Duragesic's benefits into chronic low back pain. [Unintelligible] and colleagues recently completed a study of 680 patients that took either Duragesic or a sustained release morphine for up to 13 months. The pain relief between the two groups is approximately equivalent while the Duragesic group experienced less side affects such as constipation. This was the first large scale study that also demonstrated that patients can be treated with Duragesic subsequent to only the weak opiates without first being treated with the strong short activing opiates. The value in this is those strong short acting opiates are more likely to be diverted or abused. So it may allow skipping that step. It is also important to look at the affect of Duragesic on improvement of disability. In a recent study by Cosenie and Shine looked at 131 patients across 17 centers, this study has been recently presented at the American Pain Society meeting. Treatment with Duragesic lead to a significant decrease in pain intensity as well as to fewer limitation in activities of daily life, carrying the groceries, climbing stairs, things like that. Half the patients reported significant improvement in their level

of disability being no longer dissatisfied with their physical ability. Interestingly these patients reported even with small amounts of pain relief reported large improvements in their ability, in their daily life. So taken together with the improvement in disability, chronic low back pain and our existing compendium of results Duragesic is clearly a good choice for chronic pain, for treating chronic pain, it has demonstrated low abuse relative to many other members of the class and the availability of an alternative route of administration makes it an important drug to include in your formulary. Any questions I can answer for you?

Committee: Would you comment on your recent labeling changes?

Dr. Speiser: Regarding the abuse? Those are a result of, they're a class affecting some degree, it's also a result of a few case studies that have found diversions of the patches into abuse. It's not felt to be a hugely growing problem but it is there and we need to recognize it in our label. It's a necessary labeling change but indicative of a small change that has been observed and a desire of Johnson and Johnson to make sure that people are aware of it so that it doesn't get any worse. There are cases in the literature, case reports of people ending up in the ER having chewed the patch rather than put it on the skin. That is definitely a prescription for problems.

Committee: I think you quoted two studies. I'm assuming those are studies that were not included in our material, the evidence based practices.

Dr. Speiser: That is correct because they are both very recent; one of them is only out in abstract form so that will be in your next update.

Committee: It was interesting to hear you talk about chewing. Is most of the abuse, abuse of the patch itself or by extracting, because [unintelligible] about Fentanyl in which they assured us that it was not extractable?

Dr. Speiser: By far the majority of its use, its abuse is by, there's, I won't go into these stories of the creative way that people who are desperate to abuse narcotics will find to abuse them. But certainly use of the patch either inappropriately on the skin or orally is much more common than extraction. We do know from data extracting Fentanyl from the Duragesic reservoir patch is much more difficult than extracting it from the matrix patch, that the generic patch version, but realistically that isn't probably its primary [unintelligible] abuse.

Committee: It occurred to me when we where talking about the narcotic class that perhaps we should have some public comment by somebody from the [unintelligible]. It's quite interesting in terms of creative ways in which, a lot of which [unintelligible] unique ways that they could probably educate us in terms of narcotic diversion.

Dr. Speiser: That would be very interesting and again I think you'll find that tablets are a little more easily abused than a patch in general, but it is possible to abuse any narcotic delivery system. Thank you very much.

Dr. Richard DeBose, Director of the Idaho Pain Clinic – LAOs

Dr. DeBose: My name is Dr. Richard DeBose. I am the director of the Idaho Pain Center also the president of the Idaho Pain Society which represents the majority of pain medicine physicians in the state. I understand that you are discussing the use of which opiates are going to be on the formulary for Medicaid. Just a couple things to keep in mind. First of all, as pain physicians we really only have four long acting opiates available. Sustained release Oxycodone, sustained release morphine, methadone and sustained release Fentanyl in a patch form. As pain doctors, that in itself is a problem. Generally speaking it is much better for people who have narcotic use issues to put somebody on a sustained release medicine that goes around the clock and use a limited number of short acting narcotics. Even with all things taken into account we only have four of those available. Currently on the Medicaid formulary we have three different sustained release morphine products and methadone. Both of them are good drugs, but there are some difficulties with both of them. First of all methadone can be very sedating in some patients especially in the elderly and it tends to build up in the blood stream over time as you take it. Sustained release morphine as a drug is a good drug, but many people have itching with it. And so because of that we have difficulty with some of our patients finding something they can take verses sustained release narcotic. I think most of us would very much like to see [unintelligible] patches put back on the formulary, for a couple of reasons. First of all, unlike the other two drugs

that I just mentioned they are a patch form and if you are able to put them on the patient once every 72 hours it keeps the patient from having peaks and troughs in the therapeutic levels and it also allows patients ease of use in the sense that they don't have to take an additional pill. Many patients in a pain clinic like to take pills and anything we can do to discourage that type of behavior is actually good for them. As far as abuse and diversion potential in a pain clinic we have basically a range of patients. We have patients who have only pain and no addictive type issues and another set of patients who have true addictive issues and use pain as an excuse to get medication. Those two groups are actually fairly small. What you see is a range of patients in the middle that fall somewhere between those two extremes. And we spend most of our time trying to sort out what kind of patient this is and what is in their best interest. If you look at the emergency room studies on people who come in with drug overdoses, certainly the highest drug of abuse is short acting Hydrocodone preparations mixed with alcohol. If you go back and go through all the medications that people abuse and take an overdose on, actually sustained release Fentanyl is about 92 on the list. It is very difficult to abuse because of the fact that it is suspended in alcohol and basically lipral cardboard and so patients are aware that if they abuse it that it is a life threatening issue. So as a representative of the Idaho Pain Society and also a prescriber of a lot of opiates in the state I hope that you will reconsider putting that back on the formulary. Thank you.

Question: Let's just get a clarification from somebody on the P & T committee and the Pharmacy board. I mean it's on the formulary it's just not a preferred drug or…if you're over 65 you can get it.

Committee: Right or if you have a reason that you cannot take an oral medication.

Committee: [Unintelligible] morphine or methadone.

Dr. DeBose: The problem is we have to cycle these patients through all of these other medications in order to get it approved. When a lot of times, I mean it is obvious that they are going to end up on it anyway. And so you are making us jump through a lot of hoops that we prefer that you not make us jump through in order to use this medication. It's not like we have a lot of choices anyway.

Committee: Dr. DeBose, when you say it is obvious that they are going to wind up on it anyway, what are the predictors that say…

Dr. DeBose: When you have people that like to take pills, to give them another pill to take is something that we don't want to do. And so when you have the patch you say, put this thing on, it lasts 72 hours and you don't have to take a pill. In that class of patients who is waiting for that 8 hours to wear off for them to take their next pain pill, you can break some of that behavior. In the elderly, who a lot of times forget to take their medication, these are great things for them because they don't have to remember when was it the last time I took my pain medicine and do I need it. It's a simple, place on for 72 hours write the date on it and then in three days you take it off. And so, in those two classes of patients it is actually [unintelligible] preferred treatment. It also has a much smoother onset since it doesn't really peak until about 18 to 24 hours, if you have an elderly patient that may have not been on a long acting narcotic before and your worried about how it's going to hit them, this kind of builds up slowly in their blood stream and so if they are having problems you can find that out much more quickly than if you give them a big dose of the sustained release narcotic and it's too much for them. So the nice thing about these patches is they slowly get up into the blood stream and if people are having problems they can take them off or if they are really having problems they can go to the emergency room. If they take a big slug of Oxycodone or morphine or something like that it's in there and whatever is going to happen is going to happen.

Committee: So if you are under 65 and you don't meet any of those inclusion criteria right now we don't have it where if you use one of the other long acting's then you can get the Duragesic. OK, OK.

Committee: Yeah, you can. You just have to fail one.

Question: I just wondered your thoughts, your coming to speak on behave of pain specialists, do you have any comments or thoughts as far as the general population prescribers utilizing this class.

Dr. DeBose: I think if you look at the safety and history of Duragesic it's probably one of the safer long acting medications. If you look at methadone for example, if you don't know how to write methadone you can get into a lot of trouble with it and we've seen that in Oregon already. And we are seeing that to some extent in this state where family doctors don't know the ratios or the pharmacokinetics of methadone for example then we use that a lot on Medicaid patients because it is so cheap. And it is very effective. But if you are not comfortable writing it and you don't do it a lot, patients have problems with that. Where as, I think intrinsically drugs like Duragesic are much safer just because you don't have that slow build up of metabolizing in the blood stream.

Committee: Other than someone like yourself who is a pain oriented specialist in treating people with chronic pain, do you have a feel for how much Fentanyl or how often Fentanyl is being used by the primary care physician?

Dr. DeBose: You know, I really don't. I know a number of primary care physicians use it and we would like them to use it more because in reality there's not a chance in the world all the pain patients in the state of Idaho can be managed by pain specialists. I mean it's going to primarily be done by the primary care doctors. I think if you had to choose it for safety and efficacy I mean this is probably among the safest ones that you could choose if you're a primary care doctor. It is pretty hard to get into trouble with it. Especially if you start at the lowest doses. So I don't really know how much is written by other physicians. I know pain specialist if you include everybody in the Pain Society we write more C2 narcotics than anybody in the state. If you take all pain specialist together. But there's lots of other people writing it too.

Committee: One thing that we see a great deal of is prescribing at Q 48 hours rather than the 72 hours. Where do you see that place and how is that affected?

Dr. DeBose: Well, despite what Janssen says there is a [unintelligible] where the thing just doesn't last 72 hours. And I've never really been able to get a straight answer as to why that is, but you see that. We see it in our patient population. People come in and say, boy for two days I was great but halfway through the second day I was withdrawing. And we end up putting people on it every 48 hours. We never use it more than every 48 hours, although I've seen that done. That's not a very good idea. But I don't know if these people are just quick metabolizers or what the issues are, but that's a very, it's not a common thing; you see it enough that we do it.

Committee: Do you think that's due to the fat deposit or lack of it?

Dr. DeBose: I don't know. Because the way Duragesic, at least the way Duragesic works is the amount you get depends on the surface area of the patch itself. I mean there's an extraordinary amount of Fentanyl in the patch and depending on how big a surface area you put it on that's how much you get. Some people [unintelligible] sophisticated enough to figure out how to bypass that [unintelligible]. I just don't know, I don't know how that works. But some people seem to go through it faster than others.

Question: Have you had patients that have problems, with younger patients we have a lot of problems with them falling off and coming off. How do you deal with that?

Dr. DeBose: Well I mean, there are a couple of things you can do, first of all, we spend a lot of time teaching people about how to put the patch on and where to put it on. Also if you defat the skin with alcohol or so other, acetone or something like that, that helps. The other thing we will do is in patients who have skin reactions or where the stuff really doesn't stick you can take a steroid inhaler and actually spray it on the skin where you're going to put the patch, and then put the patch over it. And that stops the inflammation associated, almost always stops the inflammatory response associated with the patch adhesive. But you can use tincture of Benzonene around the edges, you can use Tegaderm over the top of it, I mean if you really want to get the thing to stick you can do it. You have to fiddle sometimes, but we can almost always make them work if we wanted to. Thank you.

Dr. Robert Lee – Antiplatelet

Dr. Lee: I just wanted to mention a couple things about Plavix or Clopidogrel as an Antiplatelet agent. The use of Plavix has really exploded since we've started to use stents and even more so with the drug eluding stents. The data I think is pretty good there's the CURE data specifically PCI CURE which supports the use of Plavix out to at least 9 months and probably 12 months and if you look at the Kaplan Myer curves they, at the end of their study at 12 months it looks like these curves continue to split, so it looks as if there is a continuing benefit with the use of Plavix out late. It's clearly beneficial in patients with acute coronary syndromes and acute myocardial infarctions. In our community here those patients almost always get angioplasty, stenting or PCI and so those patients also probably fall into the CURE category. The other issue is for long term use of Plavix is now with drug eluding stents we're getting more and more reports of late stent thrombosis. So these patients have a drug eluding stent placed, they do very well for the first six months to a year or however long they're on the Plavix, the Plavix is discontinued, they have a sudden stent occlusion which is typically life threatening. So I think there is data and there is a lot of anecdotal data information also that supports the use of long term Plavix and as far as the use of Plavix over some of the other drugs, specifically Ticlodapine, there is just no comparison because Ticlodapine has, the monitoring is awful to have a patient come in to have a CBC every two weeks for six months to a year is just not a real option so I think that I would like you to consider allowing Plavix to be used for at least a year and if not indefinitely particularly in patients with PCI. Questions?

Committee: So you're including people that have suffered an acute coronary syndrome, haven't had an intervention necessarily in that group also.

Dr. Lee: That's I think CREDO, I'm terrible with the acronyms for these studies, but those are carried to a year so I think that for those patients it's, the data clearing supports use out to a year.

Mark Haumschild, Sanofi-Aventl – Antiplatelet (Plavix)

Mr. Haumschild: Thank you Mr. Chairman and P&T Committee for allowing me to make some comments concerning Plavix. My name is Mark Haumschild I'm a national medical manager with Sanofi-Aventis and I'm here to speak to you on Plavix. Plavix is a medication that has demonstrated efficacy in the coronary, the cerebral, and the peripheral circulation. This is important as atherosclerosis is an ongoing, inflammatory systemic disease that effects the coronary, cerebral and peripheral circulation. It has been shown that a person suffering from a single manifestation of atherosclerosis is at risk of a life threatening event caused by the same underlying process in any one of these vascular beds. In the CAPRI trial of 19,185 patients approximately 26 % had ischemic vascular disease in two or more beds demonstrating the generalized nature of atherosclerosis. Now the CAPRI trial which was Clopidogrel vs. aspirin in patients at risk for ischemic events. This was a comparison of Plavix to aspirin. The patients were followed for a period of from one to three years with a composite end point of MI, stroke, or vascular death. Clopidogrel showed an 8.7% relative risk reduction in these 19,000 patients. Thus Clopidogrel demonstrated it was more effective than aspirin in long term administration up to three years to reduce thrombotic events. Another trial we have in cardiology was the CURE trial and I understand you've heard some comments on that. That's the Clopidogrel in unstable angina to prevent recurrent ischemic events. It was a comparison if Plavix to placebo. All the patients had aspirin and standard therapies. It was a one year multi center trial with 12, 562 patients with ACS. Now ACS was defined in the study as unstable angina [unintelligible] MI, that part of the continuum. Patients received standard therapy along with Clopidogrel as I mentioned. Clopidogrel and aspirin reduced the relative risk of [unintelligible] death, stroke and non fatal MI by 20%. The results therefore were really the basis upon how the FDA gave us our indication in unstable angina. Along with that indication really came the approval of ACC and AHA as a class 1 guideline and that's, the reason I'm going to really refer to the guidelines is that they had four bullet point that they put forward. The first was in the non-interventional patients they say that Clopidogrel should be added to aspirin as soon as possible on admission and administered for at least a month and up to nine months. In terms of PCI patients Clopidogrel should be started and continued at least one month and up to nine months for those patients that are not high risk for bleeding. In terms of long term therapy, and I'm referring here now to unstable angina and non [unintelligible] patients the combination of aspirin and Clopidogrel is recommended for nine months. And the in CABG patients the drug should be held anywhere from five to seven days prior to the surgery. So those are the ACC, AHA recommendations, their class 1 recommendations. Then I wanted to make a mention to you that PCI CURE study that was where we took a subpopulation of the CURE trial for those patients that went to PCI. This is where we did Clopidogrel pretreatment or preload plus aspirin to see if it was more effective than aspirin alone in preventing major ischemic events within the first 30 days, then there was a second part where they looked as it going out as far as a year. The results were over the first 30 days the patients that received pretreatment with Clopidogrel and aspirin and there was a 30% relative risk reduction at 30 days and then when they looked at this the long term effect going out for one year it still maintained the 30% relative risk reduction. Now, I wanted to touch on, since we, since this is a Medicaid meeting and it deals with

pharmacoeconomics I did want to make a few comments in that area. And you know that the annual cost of cardiovascular disease is now approaching about 368 billion a year and that includes direct costs and indirect costs. In terms of myocardial infarction, and I will be referring back to these three vascular beds, the short term cost are anywhere from about 16 to 18 thousand, and then when you look over the long term consequences up to about 10 years it's about 45 thousand dollars. When you look at stroke in the short term, it's about anywhere from about 10 to 16 thousand dollars and in the long term, which they consider 5 years, that goes anywhere from about 20 thousand to 80 thousand dollars. And in peripheral arterial disease the cost is about 15 thousand dollars in the short term. So there's a significant consequence attached to these drug therapies. There were recently two pharmacoeconomic studies that dealt with Clopidogrel or Plavix and one was by Whytrob, it was published last year in 2004, and what they said was adding Clopidogrel to aspirin is favorable in a cost effective manner when comparing it to other cardiovascular therapies. And they also said in the patients that were undergoing PCI it was also very cost effective and they actually termed it dominant in cost savings. Then there was one other study that was cost effectiveness ratios for cardiovascular interventions. And the bottom line to this study was that Clopidogrel was competitive with Beta Blocker in cost for cardiovascular disease and actually was, how did they term, was more cost effective than the Statins. So there's two trials out there, two studies out there right now from a pharmacoeconomic point of view. My conclusions to you are that Plavix gives patients proven protection from thrombotic events day after day in all three vascular beds the coronary, the cerebral, and the peripheral. The benefits were seen early and were maintained long term up to one year. This was basically seen in the CURE study. Life threatening bleeds were not significant and major bleeding rates dose dependant on the aspirin. The efficacy of the Plavix was independent of the aspirin in the results that I have shared with you. And finally I did want to say that we saw the document that was posted from the Oregon evidence based medicine group and I would like to say that the 227 page drug class review on new antiplatelet agents that was developed by that group has been thoroughly reviewed by our organization. And that we deem that's kind of our social and professional responsibility to look at all information that is passed out that discusses our medications. After the review of the document we contacted the Oregon group and Dr. John Santa, because we had concerns about potential omissions or inaccuracies in the document. We currently have an appointment with them on July 28th to speak with Dr. Santa and the Oregon group, as he said they want to make sure the document is as complete and accurate as possible. Thank you for your time your consideration in listening to my public comment and I ask that you consider continued use of Plavix and I very much appreciate you putting up with my tardiness, travel these days gets to be kind of tough when they cancel flights on you all the time. Thank you so much.