

## Pharmacy and Therapeutics Committee Meeting Record

**Date:** 5/21/04 **Time:** 9:00 a.m. – 4:00 p.m. **Location:** 3232 Elder Street, Conference Room D **Moderator:** Thomas R. Young, M.D.

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

Agenda Item	Presenter	Outcome/Action	Assigned	Due
<p><b>CALL TO ORDER</b></p> <ul style="list-style-type: none"> <li>• <b>Roll Call</b></li> <li>• <b>Reading of Confidentiality Statement</b></li> <li>• <b>Approval of Minutes from March 19, 2004, Meeting</b></li> <li>• <b>Discussion of Key Questions for Upcoming EPC Drug Effectiveness Review Studies</b></li> <li>• <b>Review of SmartPA Rules for Long-Acting Opioids</b></li> </ul>	<p>Thomas R. Young, M.D.</p>	<p>Dr. Young called the roll.</p> <p>The confidentiality statement was read by Dr. Young.</p> <p>The minutes from the March 19, 2004, Committee meeting were approved with one change and attachment of one document.</p> <p>The key questions for ADHD were discussed at the last conference call with the Center for Evidence Based Policy. Tami Eide and Steve Montamat participated in the call. Dr. Pines provided input prior to the call that was included in the discussion. There was a lot of response to include people over the age of 18, not just children under age 18. One item they wanted to add to the effectiveness outcomes would be onset of effectiveness. They will be looking at the differences between extended release and non-extended release. Traumatic Brain Injury patients will also be included if they are diagnosed with ADD or ADHD. The Committee suggested that patients with bipolar and fetal alcohol syndrome also be included in the study.</p> <p>A handout was distributed that explained the SmartPA rules for the long-acting opioids. This handout lists the requirements for non-preferred medications. Anything that can be automatic will be and any others will be listed on a physician form. The quantity limits came from the manufacturer recommendations; however this can be overridden if clinical data is received. There was a question on the impact on savings if current patients on long-acting opioids were grandfathered. <b>ACTION: The Pharmacy Unit will use the rules provided and review current patients. This information will be provided at the next</b></p>		

Agenda Item	Presenter	Outcome/Action	Assigned	Due
<ul style="list-style-type: none"> <li>• <b>EPAP Implementation Update</b> <ul style="list-style-type: none"> <li>– <b>Statin Update</b></li> </ul> </li>   <li>• <b>DUR Update</b> <ul style="list-style-type: none"> <li>– <b>Skeletal Muscle Relaxant Intervention</b></li> </ul> </li>   <li>• <b>Drug Tracking</b></li> </ul>		<p><b>Committee meeting. The Committee would also like the DUR Board to develop educational material for this class of drugs to be sent to pharmacists and physicians.</b></p> <p>The results of the latest statin review will be available at the end of the month. The Committee will then review this data with reevaluation and contracting following.</p> <p>The DUR responded to the request for an educational leaflet on the safety issues and potential for abuse of the skeletal muscle relaxants. A survey has also been sent out to physicians regarding what skeletal muscle relaxants they frequently prescribe and why. The results should be available in June. The follow up is anticipated to be in six months.</p> <p>Mr. Markuson presented information on the Board of Pharmacy Drug Tracking database. This presentation included number of profile requests by practitioners and has proved to be a valuable tool. The database allows for the tracking of trends for certain drugs and shows increase or decrease in prescribed use.</p>		
<p><b>DRUG CLASS REVIEW</b></p> <ul style="list-style-type: none"> <li>• <b>Urinary Incontinence</b></li> </ul>	Tami Eide, Pharm.D., BCPS, FASHP	<p>Dr. Eide presented information explaining the review of urinary incontinence drugs including indications, how the drugs work, the drug-drug interactions, and availability and dosing. This review included the following drugs:</p> <ul style="list-style-type: none"> <li>• Flavoxate</li> <li>• Oxybutynin</li> <li>• Tolterodine</li> </ul>		
<p><b>REVIEW OF CLINICAL DATA</b></p> <ul style="list-style-type: none"> <li>• <b>Urinary Incontinence</b></li> </ul>	Marian McDonagh, Pharm.D.	<p>Dr. McDonagh attended via conference call and presented information explaining the clinical data of urinary incontinence drugs including the study's conclusions. This report was updated in January 2004. A copy of the information discussed was included in Committee member packets.</p>		
<p><b>DRUG CLASS REVIEW</b></p>	Tami Eide, Pharm.D., BCPS, FASHP			

Agenda Item	Presenter	Outcome/Action	Assigned	Due
<ul style="list-style-type: none"> <li>• <b>Oral Hypoglycemics</b></li> </ul>		<p>Dr. Eide presented information explaining the review of oral hypoglycemic agents including indications, how the drugs work, the drug-drug interactions, and availability and dosing. This review included the following drugs:</p> <p>First and Second Generation Sulfonylureas:</p> <ul style="list-style-type: none"> <li>• Acetohexamide</li> <li>• Chlorpropamide</li> <li>• Tolazamide</li> <li>• Tolbutamide</li> <li>• Glipizide</li> <li>• Glyburide Nonmicronized</li> <li>• Glyburide Micronized</li> <li>• Glimepiride</li> </ul> <p>Meglitinides (Oral Secretogues):</p> <ul style="list-style-type: none"> <li>• Repaglinide</li> <li>• Nateglinide</li> </ul>		
<p><b>REVIEW OF CLINICAL DATA</b></p> <ul style="list-style-type: none"> <li>• <b>Oral Hypoglycemics</b></li> </ul>	Mark Helfand, M.D.	<p>Dr. Helfand attended via conference call and presented information explaining the clinical data of oral hypoglycemics drugs including the study's conclusions. This report was updated in November 2003. A copy of the information discussed was included in Committee member packets.</p>		
<p><b>DRUG CLASS REVIEW</b></p> <ul style="list-style-type: none"> <li>• <b>Estrogens</b></li> </ul>	Tami Eide, Pharm.D., BCPS, FASHP	<p>Dr. Eide presented slides explaining the review of estrogens including indications, how the drugs work , the drug-drug interactions, and availability and dosing, this review included the following drugs:</p> <ul style="list-style-type: none"> <li>• Estradiol, oral</li> <li>• Estradiol, transdermal</li> <li>• Estradiol vaginal</li> <li>• Conjugated equine estrogen</li> <li>• Synthetic conjugated estrogen</li> <li>• Esterified estrogen</li> <li>• Estropipate</li> </ul>		
<p><b>REVIEW OF CLINICAL DATA</b></p>	Marian McDonagh, Pharm.D.			

Agenda Item	Presenter	Outcome/Action	Assigned	Due
<ul style="list-style-type: none"> <li>• Estrogens</li> </ul>		<p>Dr. McDonagh attended via conference call and presented information explaining the clinical data of estrogens including the study's conclusions. This report was updated in November 2003. A copy of the information discussed was included in Committee member packets.</p>		
<p><b>PUBLIC COMMENT PERIOD</b></p>	<p>Thomas R. Young, M.D.</p>	<p>Seven people were listed to speak during the public comment period. Public comment was received from the following:</p> <ul style="list-style-type: none"> <li>• Marcia Coleman, M.D., Wyeth – Estrogens</li> <li>• Dr. Roosevelt, Endocrinologist, and Dr. Mader, Aventis – Oral hypoglycemics</li> <li>• William Zachok, Ortho-McNeil – Urinary incontinence</li> <li>• Donald Walker, M.D., Urologist (Pfizer) – Urinary incontinence</li> <li>• Sheri Dodd, Janssen Pharmaceutical – Long-acting opioids</li> <li>• Donald Stritzki, M.D., Urologist (Pfizer) – Urinary incontinence</li> <li>• Dr. Beverly Ludders (Berlex) - Estrogens</li> </ul>		
<p><b>COMMITTEE RECOMMENDATION FOR SELECTED THERAPEUTIC CLASSES</b></p>	<p>Thomas R. Young, M.D.</p>	<p><u>Urinary Incontinence</u> The Committee determined that a long-acting version within the class should be available as a preferred choice. However, the patch and flavoxade should have parameters built in for prior authorization.</p> <p><u>Oral Hypoglycemics</u> The Committee determined that all the drugs in this class are equally efficacious and the Committee would like to review utilization prior to making their recommendation.</p> <p><u>Estrogens</u> The Committee determined that all the drugs in this class are equally efficacious and the Committee feels there needs to be a variety as preferred agents.</p>		
<p><b>SUPPLEMENTAL REBATE INFORMATION (CLOSED TO PUBLIC)</b></p>	<p>Shawna Kittridge, MHS, RPh</p>	<p>Shawna Kittridge presented supplemental rebate information to the Committee members for their review and discussion. This review and discussion was closed to the public.</p>		
<p><b>COMMITTEE FINAL RECOMMENDATION FOR THERAPEUTIC CLASSES</b></p>	<p>Thomas R. Young, M.D.</p>	<p>In the urinary incontinence class, the Committee recommends the preferred agents as generic Oxybutin, Ditropan XL, Oxytrol, and Detrol. The other drugs will be</p>		

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		<p>prior authorized.</p> <p>In the oral hypoglycemics class, the Committee recommends not maintaining a preferred agent and the brand/generic PA rules be utilized for cost containment.</p> <p>In the estrogens class, the Committee recommends not maintaining a preferred agent and the brand/generic PA rules be utilized for cost containment.</p>		
<b>ADJOURN COMMITTEE MEETING</b>	Thomas R. Young, M.D.	<p>Committee member James Schroeder, physician assistant representative, has been deployed to Iraq. The Committee wishes him well. A list of names has been obtained from the Idaho Medical Association through the Physician Assistants Association and Mr. Schroeder's replacement will be in attendance at the next Committee meeting.</p> <p>The next groups of drugs to be reviewed by the Pharmacy and Therapeutics Committee on July 16, 2004, will be beta blockers and ARBs.</p>		

**Pharmacy and Therapeutics Committee  
Public Comment  
May 21, 2004**

Marcia Coleman, M.D. - Wyeth

Dr. Coleman: I'm Dr. Coleman. Marcia Coleman. I am the Vice President of Global Medical Affairs with Wyeth Pharmaceuticals. It's great to be here today to talk to you about estrogen therapy. I am a board-certified obstetrician/gynecologist with 16 years of clinical practice experience before joining Wyeth eight years ago and I spent that in both HMO and academic practice.

I want to tell you a little bit about estrogen therapy. I was told that some of you are family practitioners, but there's not OB/GYNs here. So just to review quickly why do women take estrogen therapy. Well if you recall, remember that two-thirds of women who take menopausal estrogen therapy, you probably saw this in your review, are on estrogen-only therapy and that is because they have undergone, at a minimum, a hysterectomy whether or not they have one or both ovaries left. There is about 600,000 hysterectomies being done per year in this country and that number hasn't changed much in the last 20 years actually, although as the population ages, we think it might go up. Hysterectomies are most commonly done in the fifth decade, in the 40s, and the primary diagnosis is myelin uteri or fibroid. That's still the number one leading cause for a hysterectomy. A third of the women who take estrogens have not had a hysterectomy and, although you're not dealing with the combination products that you'd mentioned today, those women must take a progestin with the estrogen because it was shown in the late 60s, early 70s at the University of Washington, by the way, where I trained, by the Smiths, that there was an eight-fold increase risk of endometrial parcinoma in women who took unopposed estrogen with an intact uterus. So now, of course, we know as we are FDA labeled that all women with an intact uteri's must take an adequate dose of progestin and that's a very important issue, the adequate dose, because that's changed greatly over the years that I've been in practice.

When I was in training, Premarin was the only estrogen that there was available and, of course, we have many more since then. Premarin is over 60 years old, as you may know, and it was approved, what you may not know, prior to the current FDA approval process and despite that, Wyeth has invested in it, making it now the best studied estrogen on the market in the U.S. or anywhere in the world. And, indeed, to the point of the osteoporosis prevention, Dr. Young, that you were suggesting, and the women from Oregon showed in her slides, we are now the only estrogen on the market that has hip fracture prevention data and, of course, while all osteoporotic fractures are important, it is hip fracture that is the most costly for the U.S. health system and the most disabling for women. Twenty-five percent of women die within one year of a hip fracture and another thirty percent never live independently again. So it's a devastating illness.

Now, you all know that since the first publication from the Women's Health Initiative, NIH, in July of 2002, there has been a change in recommendations on menopausal estrogen use. The Food and Drug Administration, my professional society – the American College of Obstetricians and Gynecologists, and the North American Menopause Society, among others, now recommend that menopausal estrogens be used at the lowest perfective dose for the shortest duration consistent with the individual woman's needs and goals. And that individualization is very, very important, I can tell you as a former practitioner of long standing, that it's idiosyncratic what dose a women needs and for how long. It's very difficult to tell. Premarin has the greatest range of doses available; you may or may not know, from .3 to 1.25. We have recently discontinued our 2.5 milligram dose that was on there. We also, to speak to the combination products which you brought up, Prempro now has the lowest dose of progestin that has been clinically proven to protect the endometrium, which is 1.5 milligrams of mydroxy progesterone atate. That is not commercially available as itself. NPA is available at 2.5, not 1.5. So if you think about the combination products, it's the only way that women can get the lowest dose known to effectively protect the endometrium. We are aware of your population, 60 percent of Idaho Medicaid women who take an estrogen product for menopause, take a Premarin product.

I really was going to stop there, I thought I only had five minutes and was going to answer questions so I'd be happy to entertain any questions. There were several points brought up with the slides with questions about HERS, for instance, that of course I'm very familiar and of course the WHI that I could answer questions about if you'd like.

Dr. Montamat: Since you bring up that one, the idea of improved in eliminating or lowering cardiovascular risk, I mean, certainly those studies recently have suggested that we're seeing greater cardiovascular risk in certain populations of women. What are the studies...

Dr. Coleman: I'd be happy to address that because it is very confusing and since WHI's been published, the E plus B arm anyway, a lot of people have said, "Well, how could all those epidemiological and observational studies suggest lowered cardiac risk and yet WHI-E plus B show an increased risk." I think there's several ways to look at it. First, when all this data started coming out epidemiologically, Wyeth decided that a secondary prevention trial might give us a better idea so HERS was begun. It was a secondary prevention trial, the average age was in the 70s, all women had either a documented MI or angiographically proven synosis, whatever, and we clearly saw in HERS that there was an increased number of events in the first year absolutely. What you were asking about, the conflicting information from it is that when you follow those people out with the HERS-2 extension trial, at the end of six years it showed no difference between the estrogen or progesterone treatment patient and placebo. So it appear also in the WHI E plus B arm early on, the DSM being notified women on the products, that there had seen an excess number of cardiac events in the first year and actually we put it into our label at that time. What we've seen now is the E plus B arm did show an increase incidence, the WHI-E alone arm, just published, did not show an incidence. And remember, the NIH designed these trials to show that it was protective. They believed it was protective based on the epidemiological data.

Now, why is there a difference? Well, if you look at the populations, you might see this. And I just heard Dr. Leon Spearoff, who is sort of, if any of you know him, he's at University of Oregon at the—and he was former chair of OB/GYN there and he's sort of the "guru" in reproductive endocrinology. He was talking about it's the population that's different and the epidemiological studies, many of them followed women from much earlier on, such as the Nurses Health Study where women were 30 to 55 at enrollment, versus in the WHI where women were at 50 to 79 and only a third of the population was between 50 and 59, which is the age you might think about women going on \_\_\_\_\_, and there is definitely some evidence that when you develop avlothrosis, the estrogen receptors in the endothelia lining decrease so if you have established disease, you won't have a receptor there so if there is a beneficial affect, you won't have it.

Any other questions in my quarter of a minute? I still have half. Thank you.

Steven Roosevelt, MD. - Aventis

Dr. Roosevelt: I'm going to ask leave—I'm having some things copied and I'll just ask leave to have those introduced at the end of the discussion if that information is duplicated.

What I'm going to tell you is the following. I was kind of interested in the...

Dr. Young: Would you introduce yourself, who you represent, who you are being remunerated by, that sort of thing.

Mr. Mader: Jake Mader with Aventis Pharmaceuticals and we were here along with Dr. Roosevelt to present on Amaryl. So if you have any questions, particularly for him or the state government affairs prospective, I'll be here to answer any of those questions. Pat Lind was here originally but we are making some copies right now.

Dr. Roosevelt: Steven Roosevelt, University of Utah in 1974 with a Ph.D. in Don Nelson's Lab, did an endocrit fellowship at Harvey UCLA in Bill O'Dell's Lab, private practice Southern California in 1979 to 1993, moved to Boise 1993 to present, been in practice, affiliated on the medical staff at St. Luke's and St. Luke's Meridian. Private practice by myself, currently board-certified and have been in endocrinology since 1983 and internal medicine since 1977 when I finished my

internship and residency. I have been remunerated by Aventis since the schedule was up—Pat bought me a Super Scramble at Denny's this morning, but otherwise I'm not getting anything for this.

The data that was presented to you, especially the Oregon Health data, needs to be put in the proper perspective and the perspective is the natural history of diabetes. Now the physician members have seen this slide ad nauseam; however, many of you may not have seen this slide. This slide depicts the natural history of diabetes, Type II diabetes. As you can see, the patients present initially with insulin resistance which is followed by a compensatory increase in beta cell function and insulin output. After awhile, however, because of a variety of reasons, beta cell failure begins to occur and then dysglycemia occurs. It's not until sometime after beta cell failure begins to begin, however, that the clinical diagnosis of Type II diabetes is made. We now from the U.K. PDS and \_\_\_\_\_ PDS discussion today that glycemic separation is possible with conventional but intensive therapy, but the other thing to take home from the U.K. PDS is that this Nike "swish" curve shows a progressive increase in A1C overtime, regardless of treatment modality and the reason for that is that there is a progressive decline in beta cell function before and after the diagnosis. What does this mean as far as all the data that you were presented today on comparative studies? Well, it means that even if the patients were matched by age, sex, race, time of diagnosis, that all of those patients had differing slopes on beta cell failure curve and all of those patients were at a different point in the beta cell function decline curve because sulfonylureas in med form and insulin do not have any affect upon these curves. Okay, so although the patients seem comparable, they're not because they may have been, but we don't know that. So that the data that the Oregon people presented to you are not as solid as they would have you believe because on the natural history of diabetes, we don't know if they presented with the same percent beta cell function. Are you following me? Excellent.

So if the drug studies are not comparable, then according to your mission statement, you're not interested in anything except quality of care. Okay? Quality of care, and there's some papers that were presented to you as well as this one, indicates that there is a substantive difference between Glimpiride and the other sulfonylureas in that Glimpiride stimulates first phase insulin secretion, Glyburide doesn't. Glimpiride has a beneficial, or at least a non-deleterious affect of con-cardiac preconditioning which the other earlier sulfonylureas don't. One of the things that she talked about was that black box warning that's on all sulfonylureas from the UGDP. I'm old enough to have prescribed Phenphormin when it was the byglonide that was around and I'm old enough to have prescribed Toludase and Diepanese. Okay? And we did that with a certain degree of caution, especially after UGDP was published because we're all like, "Well, what does this mean, what does this mean?" What it doesn't mean is that the degree of glycemic control was different in those two groups, insulin and sulfonylurea on the UGDP so they've never figured out what it meant. What they're thinking now in retrospect is that the patients on sulfonylureas did not have ischemic preconditioning or it was blunted by virtual of the fact that they were on a drug which seemed to prevent that. Now, do I have any hard clinical data like that? No, I do not. I'm going to be honest with. I'm not going to tell you, you know, fill you up with a bunch of stuff, but we do know also and I just handed something out that treating patients with Glyburide and Metphormin over a long period of time increases cardiovascular mortality. Okay? Type II diabetes appears to be a disease of myocardial dysfunction. The skeletal muscle and probably the myocardial muscle in patients with Type II diabetes, they're myacondria are smaller and less efficient. Both Metphormin and Glyburide have adverse affects, which you can get out of those papers that were presented to you, upon myocardial function. So, like Metphormin poisons your myocardial palasites, that how it prevents gluconeogenesis. Sulfonylureas, although they have a deleterious or a beneficial effect upon insulin secretion, seem to have, with the exception of Glimpiride, a deleterious affect upon myocardial function and skeletal muscle.

What I'm asking you to do is to consider the fact that if you have a preferred drug list which does not include Glimpiride, which I'm almost convinced that that is distinction without a difference, alright, that it's going to make it much more difficult for those of us in the endocrine community who are practicing, you know, kind of what we feel is the standard of care for diabetes management in this State, to take care of Medicaid patients to begin with. I'm the only physician in Boise who takes care of Medicaid diabetics, okay, except—I'm the only endocrinologist who takes care of Medicaid diabetics. Steve takes care of—you guys take care of them, but I'm the only endocrinologist that does. It's going to make it much more difficult for me if I have to write you a letter to prescribe Glimpiride for these patients because of what I feel are convincing but not yet provable data for treating these patients. The other thing to consider is although this is a burden upon taxpayers, the actual burden for diabetes management is, to a very large part, not incurred in the outpatient setting. We know that 70 percent of the cost of a treating a diabetes patient occurs at St. Luke's, not at SLM, not in my office, not in your offices. Okay? And drugs are only half of that.

Physicians' fees and lab tests and the other stuff is the other half of that. So as a percentage of the whole diabetes budget, the medication is actually relatively small. Okay?

Now, I'm going to close with one statement. Bismark once famously remarked that there's two things you don't want to see—sausage being made and legislation being made. Okay? And I sometimes think that administrative rules are in the same category as sausage and legislation. If you have any questions, I'd be happy to answer them.

Dr. Montamat: Steve, on one of the articles that I received and it's definitely, you know, supportive of Glimepiride, and they talk about that the recent data from the U.K. PDS, the more recent one, found no enhancement of cardiovascular events or mortality by treatment with sulfonylureas and, instead, there was a trend towards protection against myocardial infarction so would you propose that Glimepiride would even give better protection? Because it seems to me that the old one...

Dr. Roosevelt: It was Diepanese and Glyburide that were used in the U.K. PDS. I don't know that for sure, but here's the other possibility against this. There is a legal doctorate--in addition to everything else, I happen to be a lawyer—and there is a—I can't think of the name of it right now, but, you know if the drug company—it's there to protect drug companies and it's probably there to protect the decisions that you—oh, it's the Informed Intermediary Doctrine. The Informed Intermediary Doctrine speaks to this, if the doctor prescribes something and he's been told that it's dangerous to do it, he goes out and does it then the vendor is off the hook. You know, this isn't a universal jurisdictional rule, but it is in some jurisdictions, you see what I'm saying? So if you write for Regelin or you did write for Regelin and you'd been told by Parke-Davis that Regelin was inherently dangerous, if you have all the data which physicians were blinded to—we had no idea how bad things were going on the Regelin data until they jerked it off the market—do you see what I'm saying? But if all that data had been given to you and you continued to write for Regelin, you'd be on the hook for putting your patient at risk and Parke-Davis would have been off the hook.

Dr. Montamat: Here's the point I'm trying to make, in this editorial they're saying that there's actually less myocardial or cardiovascular events and so are we to take the testimony to say that Glimepiride, it's not that it's subtracting from cardiovascular death or if it's actually just better. I don't—I think it's an important point.

Dr. Roosevelt: Yeah, that would be my conclusion based on the data that's available. As I told you a few minutes ago, you know, you can't do a controlled study on this. The last paper that was handed out speaks to the fact that Glimepiride and Metphormen was a very dangerous combination in diabetes patients, probably because Glyburide and Metphormen are both myocardial poisons.

William Zachok – Ortho-McNeil

Mr. Zachok: My name is William Zachok. I'm here as an employee of Ortho-McNeil Pharmaceutical to discuss the overactive bladder/incontinence category. We appreciate Dr. McDonagh's report and OHSU, but there are a few distinctions we would like to point out in that report.

First is that in the report, Dr. McDonagh did not reference the updated BEERs criteria. And just as a review, the BEERs criteria is a list of medications which are deemed inappropriate for use in the elderly. This publication is put out by an independent panel claiming no financial interest in any of the medications which they discuss. The BEERs criteria was updated last year and they do not only make a distinction between immediate release agents in this category versus the extended release agents in this category, recognizing that they are two distinct entities, but they specifically go out of their way in this most recent update to point out that Ditropan XL should be excluded from the BEERs criteria in the author's words because the panel believed that the XL version had fewer side affects than the immediate release products.

The second point we would like to make is that in the OHSU report, the different indications are not necessarily addressed among the agents in this category. Ditropan XL was recently approved for use in pediatrics. Not only attesting to the diversity which physicians may pull upon this agent in the patient populations that they can use it in, but also attesting for the safety of this agent.

The final point I would like to make is that in the OHSU report, Dr. McDonagh does address the OPERA data, but we do have some differing opinions on what she views and the report views as important. In as much as overactive bladder is not a curable disease the way anti-infective would go to cure the specific organism, if you can get your patient population to dryness, I think about the self-esteem category, you give a certain amount of dignity back to these patients. If you include ancillary costs, diapers, the risk of falling, getting patients to wet—getting patients to dry who are wet would certainly be an advantage. And in that report, in the OPERA data, that was statistically significant. The Ditropan XL shows statistically significant improvement in getting the amount of patients to dry. She also points out the incidents of some side affects, specifically dry mouth, and while it's true that there was an overall higher incidence of dry mouth with Ditropan XL, if you break it down in the moderate to severe category—and by severe, the authors refer to as something that requires medical intervention or something that interferes with daily activities. If you look at the moderate to severe category, there is no statistical difference in that study.

I'd be happy to answer any questions.

(End of Tape)

Dr. Young: ...may be addressed by virtue of the way we deal with a lot of our senior citizen medications and there are special considerations given by age, location of the patient, that sort of thing and so some of those--there's criteria that we function under on the other side of the house being the auditors for the nursing home to consider. Any questions? Thank you.

Mr. Zachok: Thank you.

Donald Walker, M.D. – Pfizer

Dr. Walker: Hello. I'm Don Walker. I'm an urologist and I think I represent the hard-core low person on the totem pole. I've been in practice in Boise for almost 28 years and practiced general urology during that time period. I trained in Oregon and have been board-certified since 1978. I work at St. Luke's, St. Al's, and I also work at the VA and the VA is probably at least half of my practice. What I'm going to give you isn't a scientific thing but it's kind of my philosophy and what I think is important and kind of why I practice the way that I practice and I have preferences. I'm speaking for the anticholinergics and the drugs for treating overactive bladder.

Overactive bladder covers a wide scenario of patients, all the way from those with mild urgency to those that have neurological damage that gives them severe spastic bladders and the anticholinergics are helpful for all of them. For many of the patients, it really doesn't matter what you choose because if you—they just have mild urgency, if you're not able to solve the problem, it's not a big deal. But there are some patients where it's a big deal and if you don't resolve the overactive bladder consistently and perfectly, they can progress to damage to the upper tracts and they can progress to permanent damage to the bladder that can make future help for these people very badly or very poor. So I think it's important in certain people to have options available for you. I think the way I practice, at the VA especially, is I do use the regular Ditropan, the inexpensive material, the three times a day material, and it works for many of the people. It doesn't work as well for a lot of the people for—let me step back one thing. I think as far as efficacy, they all work reasonably well. Some of them work a little bit better than others and so to start with an inexpensive drug I think is a good philosophy and I think it will resolve the issue with the majority of people. But there are certain people that it won't resolve the issue and those are the ones that I ask you to consider having other drugs available besides the plain Ditropan.

One of them is a good number of the people that I deal with are elderly and because of the tendency for the Ditropan itself, it's creates some trouble with short-term memory loss. I don't like using plain Ditropan in my elderly patients or someone who already has Alzheimer's because I may be aggravating that problem and not really helping them and Tolterodine has a very low affinity for fat and suppress the \_\_\_\_\_ barrier in very low amounts and so it does not appear to be a problem. With the side effect of dryness of mouth is probably the biggest side effect that keeps people from being consistent in taking the drugs for long periods

of time and that's the reason that most people quit taking the medicine. At the VA, I have Ditropan that I use on the majority of the patients and then they have Tolterodine that's off the formulary that they allow me to prescribe to my patients that I feel need to have that. And the biggest reasons that I prescribe are going to be those that are elderly and I feel they have some Alzheimer component and the other group is the people that I put on the Ditropan to start and they are not compliant and it's a problem that is severe enough to where I feel that I have to have control and have to take care of it. Tolterodine is a once a day, where Ditropan—plain Ditropan is a three times a day preparation so for patient compliance, I prefer the Tolterodine and if they have the dryness of the mouth, I prefer the Tolterodine and for many of the other people, I can get by with just the plain old Ditropan.

I have this philosophy mostly because of cost and it's been a philosophy that I've had for many, many years and at the same time I feel it's important to care for the patients properly, giving them the dignity of being dry is very important. But the Ditropan is used a lot on people that just have mild urgency who are not incontinent but have a lot of frequency and urgency. The Tolterodine has been studied in men that have bladder \_\_\_\_\_ obstruction, another one of the causes for some of the urgency, and it doesn't increase residual urines and it's something that you can safely use on a person with overactive bladder and some mild bladder \_\_\_\_\_ obstruction with not being very likely to put them into retention. And my experience over the years is that they do better with Tolterodine than they do with Ditropan XL or plain Ditropan. That's my personal experience.

I have been offered to be paid by Pfizer and I am here representing them but they had no trouble getting me to come in and be willing to talk with you. Any questions?

Dr. Gundlach: If you have just mild urgency, can you take these drugs PRN?

Dr. Walker: I have a lot of patients that I will encourage them to just take it when they're going to go out. If they're at home, telling them timing going to the bathroom before their bladder gets full is sufficient. They don't need it for that. There are other patients, i.e., someone who's had a stroke who has a severe spastic bladder, has an upper motor neuron lesion, someone with Multiple Sclerosis with just brain lesions rather than spinal cord lesions who's not retaining any urine, those people have to have control of their bladder or they do damage to their upper tracts. Those I don't give a choice to. But I'd say with 60 percent of my patients, it's a choice and it's to improve their symptoms; it's not mandatory and those are the ones that I offer the drugs on a PRN basis or just to take the plain Ditropan.

Thank you.

Sheri Dodd – Janssen Pharmaceutical

Ms. Dodd: Good afternoon. My name is Sheri Dodd. I'm an epidemiologist health economist with Janssen Medical Affairs here today to talk to you. One I have to thank you for the opportunity of being here. I don't know anything about urinary incontinence or diabetes so it's been very informative. I'm here today to talk to you about long-acting opioids, the review I think you did last month.

A couple of issues, and I'm not going to beat up on the Oregon Health Science process. I don't know if you've had that as you go through this. Obviously you understand the limitations. I presented and spoke at the Oregon meeting and it's very clear to me that their process is from a good place and they do include the randomized controlled trials and they do have a high grading. What's not included, I'm sure you know, are posters—scientific posters, case reports, documentation put out by forensic units, and epidemiological surveys that don't hit the peer review literature. Why that's problematic is because a lot of the data on the long-acting opioids is bubbling up through other sources that you're not finding in your journals of pain, etc. And one of key issues and one I deal a lot about is Methadone and the fact that Methadone was included in that long-acting review as being comparable to the other branded opioid products, but actually there was not evidence. So lack of evidence actually made them equal and they're lower cost.

Along with Methadone, and if you look at the drug early warning systems, the increased use of Methadone has caused many outbreaks and, as some have said, many epidemics of fatality, mortality for non-abusers. So this is chronic, non-malignant pain users who have been forced to use Methadone first-line by their primary care physicians because of formulary policy decision-makings and actually have died. There's a long half-life with Methadone. It is very difficult to titrate. It's very difficult to treat with and there is no drug rep out promoting the use of Methadone because it's not a friendly product. So by promoting the use of Methadone as first-line knowing that majority of the scripts for opioids are written by primary care physicians, I think sets up, not to be dramatic but, a disaster. And if you go to Oregon, Florida, the Eastern Seaboard, this is what's occurring. When I was at Oregon and we brought this up, they were very concerned but unfortunately the process of the Oregon Health Science review is not to include these type of data. They don't have a way of processing this in their review.

So as you review the dossier from Oregon and you look at these, I would just encourage you to incorporate other types of data. It's difficult, um, but it's out there and Oregon has looked at it and they are re-reviewing their process of inclusion for studies so they can pick this up. They have a way of looking at safety. Nobody's funding a study on safety in Methadone so it's not going to show up in the literature even if it's out there and is being reported. So our concern is choice in the opioid category, offering Methadone and promoting Methadone as a first-line without good educational background for primary care physicians who really will get into trouble using it. Basically, it's problematic.

Morphine as a product has been around a long time. There's other products, duragesics, the Oxycodone long-acting products. That offer choice. Opioid rotation is common, it's practical, and it's how practitioners treat chronic pain. So it is very likely that a patient who's done well on Morphine will need a different drug at some point in time and according to this process, that's going to have to be documented and is going to have a gap in therapy.

The other thing I wanted to bring up a little bit was on continuity of care. With chronic pain patients, once they get stable they do pretty well. You get them titrated, they get to a point where they're having higher productivity and functionality. As I read the current process, any patient that's on a non-preferred product is going to have to go to a preferred product so you're going to take perfectly stable patients, make them titrate over to another product, get them up to a titration level and steady, and have them endure that period of time where they'll be maintained on that opioid. So I would try to encourage continuity of care of patients that are doing well right now on products that are not on the preferred drug list, potentially look at allowing them to stay on that product, especially for duragesic there's a wide range. It isn't that you take someone who's on a 50 patch and you transition them over to Morpedian, whatever, 40 milligrams. It isn't that easy, there's wide ranges and there'll be a lot of expense in trying to get these patients titrated and stable on a different product. We know that when patients are stable, they have good functionality, good productivity, and I hope Oregon, and I've heard on the phone Dr. Helfand saying that they're going to try to make these reviews so that they include those type of data. The long-acting opioid review did not include productivity, quality of life, functionality data in the way that these new reviews are. So I hope they're going that direction. Any questions that you have on duragesic-specific or on Methadone or the resources that are out there to kind of take a look at some of these medications.

Dr. Eide: What about the availability of like the 75 milligram, which is forcing us to use the lower doses and is really increasing the expense?

Ms. Dodd: Yeah. I just got a voicemail and I don't know if Jeff maybe knows more about from the availability, but I just got an update that the 75 should be back up to full production in two weeks and that there had been a delay on the 25, 50, and 100 and those are back up to full stock so they are able to—that's what I heard on from my state government affairs folks. Jeff, did you have any comment on the availability of the 75 patch and some of the delays that there were in stocking and supply?

Jeff: No, I don't.

Ms. Dodd: No idea? Okay. That's what I heard as of yesterday.

Dr. Young: How many Medicaid patients are on stable doses of transdermal duragesic as opposed to escalating or continuously changing?

Ms. Dodd: I'm sorry, I couldn't hear the beginning.

Dr. Young: How many—how many Medicaid patients are on continuous fixed doses of duragesic versus escalating or changing doses on a continuous basis?

Ms. Dodd: I don't know for Medicaid patients versus commercial patients, but I can tell in general we've gone back and looked at retrospective states to look at length of time on single dose but there is a ramp-up to get someone on the appropriate dose and from that, most patients can—60 percent of the patients will stay at what appears to be their final dose. There is...

Dr. Young: What happens to the other 50 percent?

Ms. Dodd: That they will either develop a tolerability to the product of which the physician can choose to try to increase or they'll switch them to another product and I think that's why choice is important. It's not so much failure of the drug; it is receptor blocking and opioid tolerance that builds up with any of the products. There's no opioid that doesn't have opioid intolerance. You'd get the same on Methadone.

Dr. Montamat: You aren't insinuating that some of the inappropriate prescribing of Methadone was due to the lack of drug reps for Methadone? That's a very interesting point.

Ms. Dodd: What I'm trying to say is that Methadone is a difficult drug to use and so if Methadone is encouraged to be used first-line by primary care physicians who have not been trained or well-versed in how to use it and how to titrate it, they could run into problems and unfortunately versus companies that do have drug reps that go in and help train on how do you titrate, there isn't anyone training physicians on how to use Methadone.

Dr. Montamat: Well hopefully there are.

Ms. Dodd: Hopefully there are?

Dr. Montamat: Pharmacology departments and medical schools that are doing some of that.

Ms. Dodd: But the rural physician in Rupert, I don't know that they're getting trained on Methadone.

Dr. Young: I think that begets the responsibility of the physician that if he's going to write a prescription for something, he is responsible for knowing how to use it and us suggesting that that's a first-line drug and a physician not knowing how to use it and going ahead and using it is to assume that the physician is not doing his job or her job.

Ms. Dodd: I would absolutely agree and I think what they found in Oregon, and in Florida, and on the Eastern Seaboard is that the directives given to use Methadone first-line, they correlated it with this increased risk in Methadone deaths and the DAWN data is also showing that increased use in Methadone—it doesn't differentiate between addict, um, for drug abuse versus others but as you are having an increased use in Methadone from the normal event perspective, you're also having an increase reporting in emergency room events. So we're learning more.

Dr. Young: We've already been to this point before, but the folks in Oregon I'm not quite sure completely bought off on the fact that the number of Methadone dose drugs over-utilizations in their ER is directly related to their policy of prescribing Methadone since they have...

Dr. Eide: They've actually shown it's not.

Dr. Young: Yeah, and the actual fact of the matter is in Oregon, the two were found not to be linked.

Ms. Dodd: It is a pretty short period of time. I mean there's an increased use in general and I'm not meant to say that it's Oregon's policy in general. There's an increased use in Methadone and there's an increased reporting of ER visits and increased death associated with normal event use. So people are watching.

Dr. Young: All we're saying is that so far the review of that that they have come out with has not linked folks together and a causal relationship will be necessary from a study standpoint to say that these two happen to be linked because, for example, even looking at the data that was shown by the Pharmacy Board here, we've had a significant increase in the use of Methadone in the State of Idaho in the last two years, no deaths associated with it, and you look at our policy. So I don't know what to make of that, but the reality is people are using it more.

Ms. Dodd: They are definitely using it more and I think time will tell and hopefully the Oregon process will allow those type of studies to be included because they wouldn't make the cut right now.

Dr. Young: Would you make the same argument then that the morphine sulfates that physicians are also not being detailed on those because and, therefore, don't know how to use those as well either and those would be dangerous choices?

Ms. Dodd: Well, no. There's...

Dr. Young: ...the long-acting morphines?

Ms. Dodd: But there's branded products with reps detailing the morphine, so no. I think it's just an educational issue. We didn't...

Dr. Young: I think it's too bad that we, as doctors, don't get any education except from drug reps.

Ms. Dodd: I'm not meant to say that. But there's no literature out there about, I mean there's just no current data on the use of Methadone and on malignant pain. The literature is very slim.

Dr. Young: I just got to tell you that makes me feel bad inside.

Ms. Dodd: Well, I...

Dr. Young: That I'm not getting any education any where...

Ms. Dodd: I \_\_\_\_\_ everything from the education on leaving people feel bad. That was not my intent. I think my intent is choice is what I'm trying to encourage.

Dr. Young: Other thoughts and questions? The rules that you have in front of you are something that we will need to talk about. We brought those to you and those are still up for discussion so if you have any questions, you need to get those out.

Dr. Montamat: In speaking to the Committee, the Oregon—the process that goes on through looking at the drugs does have some exclusions but there is reasons for that that I think are pretty valid and it's up to us to use that information and if we don't agree with it in our decision making, I mean, we use what we need to use and we

look at it for what it is. I don't know that the process is going to change that dramatically. We do look at the key questions cyclically and add different key questions but the level of evidence, I am not aware, that that is changing.

Ms. Dodd: I think what I heard Dr. Helfand saying when I looked and it had its new reviews that are coming out, they're actually broadening it and they're allowing more for patient preference, patient satisfaction, functionality, quality of life, those domains.

Dr. Montamat: Those are measure. Those are not types of studies though.

Ms. Dodd: Well, in the majority of observational studies, those are the primary endpoint.

Dr. Montamat: Most of us want to base our information on the scientific method which means reproducible results. Having a poster at a meeting is great and it can be intriguing evidence, but it needs to be followed up and it needs to be peer reviewed. I mean, to make decisions based on data that's not peer reviewed is--most of us I think would disagree with that.

Ms. Dodd: It's weight of evidence and there's a lot of evidence out there.

Dr. Montamat: Bad evidence as well as good evidence too.

Ms. Dodd: Exactly.

Dr. Montamat: When weighing that evidence, that's, you know...

Ms. Dodd: I was just at APS and there's was award-winning posters and those posters and those data will not make it into manuscript until the middle of next year. So there's a lag where there's really good data out there right now and yet you're not going to see it until next summer in publication and then it will be included in the Oregon review so you can have up to a two year lag on that data.

Dr. Montamat: And there's a reason for that, for a peer review process to take its place.

Ms. Dodd: Sure.

Dr. Young: We do have this to deal with so, like I say, I want to get...we need to get all the questions about the opioids on the table and all the concerns and all the ups and downs because it is an important topic and I think the issue that Ms. Dodd brought up about grandfathering is one that needs to be discussed and considered and looked at. Takes \_\_\_\_\_ input and Steve's and some of the people that are doing the elderly, all those pieces need to be brought in and we'll make a decision \_\_\_\_\_ and it is going to be somewhat a responsibility to provide some of that education. I talked with some of the chronic pain docs and there is certainly an awareness on their part and I think a sense of responsibility and I know Rich DuBois, I've talked to him before, would be very happy to come out and help educate people and provide some of that education about how to utilize some of these medications.

Donald Stritzki, M.D. – Pfizer

Dr. Stritzki: My name's Don Stritzki. I am receiving an honorarium from Pfizer to be here this afternoon. I'm a board-certified urologist. I practice in Caldwell and have a private practice there.

I, last year, I saw over 9,000 patient visits. Many of those patients were having problems with ditrusor instability and I have found that both Oxybutrin and Tolterodine are both very helpful and effective in treating ditrusor instability; however, the concerns about Oxybutrin and CNS affects and impaired cognitive skills are very real, it's not just theoretical. Last year, for example, I happened to see one woman who was a 33-year-old woman who had a brain tumor. She was also having problems with her bladder and ditrusor instability. Her neurologist had placed her on Oxybutrin and she needed pretty high doses to control her bladder. When I saw her, one of the major concerns that the family had was about here deteriorating mental status. She was very confused. We changed her medications and put her on Tolterodine. Her mental status cleared very quickly and dramatically. She died six months later from complications of that brain tumor, but the family was especially grateful for the improved quality of life that she experienced after we changed those medications.

Many of the patients we see are already suffering from some impairment in their cognitive skills, maybe they're starting to be demented or things like that, so there are already concerns and issues and we see that particularly in patients who are on Medicare. I would be very concerned about using medications that can exacerbate their already concerning mental status and I would strongly request that Tolterodine remain available because I think there's a real important difference.

I can answer questions if you have some.

Dr. Gundlach: Aren't there several other new drugs, probably in Phase 3 studies now, that are even going to be better than Tolterodine?

Dr. Stritzki: There is one particular new drug that last I heard was in Phase 2 study or just beginning the Phase 3 study that the preliminary data is suggesting that about 60 percent of patients will respond. So it's not going to be 90 or 100 percent. Of those patients who do respond, they will do well with fewer side affects that any of the anticholinergics that we have right now. So we are optimistic about some additional drugs. How long it will take, we're not sure but they're a ways off.

Dr. Sutton: What about the difference in immediate release and extended release efficacy and safety?

Dr. Stritzki: That's a very good question. I think that the sustained release really has some important advantages. The first thing is patient compliance. If you can have a medication that somebody takes once a day, they will usually do pretty well at that. Twice a day mostly. If it's something they have to take three or four times a day, they don't get it. They'll take it twice, sometimes once, sometimes three. So compliance becomes a real big problem. We also see that with the shorter acting medications, there are more side affects. We see more dry mouth; we see more blurred vision, and more constipation. So there are some patients who do well with immediate release, but the compliance and side affects are more of a problem.

Thank you for your time.

Beverly Ludders, M.D.

Dr. Ludders: I'm Dr. Beverly Ludders and I'm boarded in family medicine, but the past 34 years I've been doing women's health care. Let me tell you how... I am actually getting an honorarium from Berlex which deals with the Climara patch.

Let me tell you why I'm interested in the patch. In 1987, I had a hysterectomy because of a precancerous pap and I had an ovaectomy done at that time. I was amazed with the affect that it had on me and became very passionate about feeling better and at the time I used every single pill that was out there and the patch was relatively new at that time. So I'd had these dull headaches and I wouldn't have energy. I never had a hot flash, never had a hot flash, and I put the patch on and my headache started to go away. I upped the dose and was like—I felt like a different person.

So in doing women's health care for a long time, I started looking at what we were missing and I realized one of the things we were missing was depression so I got interested in depression. And as I studied about depression, I realized how hormones can have an affect in that hormones actually modulate the other neurotransmitters. I was recently, at the first of May, at the American Academy, excuse me, the American Psychiatric Association meetings in New York and I went to a meeting on women's health and they said in the perimenopausal time, there's three times greater incidents of depression in women; if they have hot flashes, it's six times greater. And I'd been seeing this but I had never heard the statistic so it reminded me of week I had three perimenopausal women and they were all depressed, never been depressed before, and these women they're talking about had never been depressed. And so what I did is I did a physical, did blood work to make sure they didn't have a thyroid problem, did not have anemia or some other medical problem, put a patch on them, and see them back in a week. The reason I like the patch for this, you start absorbing the patch in three hours and in 24 to 48 hours, the patient would notice that they're different. They sleep better. They just have this—they just start to feel better and so—and then they have control. They can just rip it off if they don't like it. I say, "Just rip it off if you don't like it for any reason." Well, I saw these women back and they were diagnosed with depression. I used the Beck depression inventory, the anxiety scales, and about three or four other scales when I need it. And they all had depression ranges and all three of them came back and that's all I needed to do.

And so, the other reasons that I like the patch is there's some very good studies that show that probably with the patch, it does not affect C-reactive proteins, which the pill does. There's some other studies that show that we probably are not affecting the \_\_\_\_\_ factors and in the Women's Health Initiative, which I feel a little bad about the Women's Health Initiative because many, many women are making decisions off of this and doctors don't know what was in the study. Do you know that the average age was 63? These women went 13 to 15 years without any hormones and they threw a pill at them and said, "Oh, we don't have very good results." And 49.9 percent of those women smoked, 34.4 percent of them had a body mass index of 30 that meant at 5'7" you weighed 190 pounds. That's not a lot of my women patients. A lot of my patients don't smoke because the doctor gets on their case. So to extrapolate that and deprive all women from hormones because you're scared. The number one reason that I see that women don't take hormones is fear. The number one reason that my patients stay on it is the sense of well being. And the reason that I favor the patch is that...I'll give you an example of one I just saw today, my very third patient. She had a gynecologist and she had a psychiatrist and she came in to me because she still didn't feel good and so I put a patch on her and I tweaked her antidepressant. Her score—you see, generally I can tell if it's hormonal versus the neurotransmitters by looking at their scores. If they're extremely high, I know they're probably going to need both a hormone change and the antidepressant changes. So I put a patch on her and I saw her back today and she's telling me all these things and I said, "Do you mind if I write these down and I quote you?" And so these are the things that she said to me. She said, "You can quote me, you can use my name." I said, "No, I won't use your name." "You can tell them that I felt like I was a raving idiot before. I can finally remember things. You don't know how bad you feel until you feel better. You lose it slowly. I'm totally amazed at the difference it made in one week. One week on the patch made a tremendous difference. I no longer am a babbling idiot. My doctor said that he didn't like the patch, but obviously he didn't have a hormone problem. It affected my job and everything that I did." And this is just one today that I had.

I guess that I'm a real believer in that we individual health care and like I tell my patients that some women swear by the patch, some women swear at the patch. So what I think we need to do is find what's going to work for that individual patient. Also, it's very difficult now to get anything positive on hormones out through the lay literature, its media driven. Do you know that the North American Menopause Society did PET scans and they took two groups of women who were 50, most of them were in the perimenopausal phase, and so they did PET scans on the brain. The PET scans actually show a flow of blood to the different areas of the brain and they looked at the hippocampus. The hippocampus is the area of the brain where we have our memory. And what they found—and also where they get Alzheimer's, it would be a diminishing of the hippocampus—in the women on the estrogen replacement had a larger hippocampus; it was atrophied in the women not on estrogen. What I see so often with my patients that use the patch, I think they get a more consistent absorption. Now, I don't push anything; if someone doesn't want to use it, but I really think we need to have a good patch that we can use. I know what a difference it made for me.

Just a quick story, I have an identical twin sister who is a doc and she had not had a hysterectomy. She was 51 at the time and was having regular periods and she called me and she sounded down on the phone and she didn't have much energy. I said, "Put a patch on and call me in a couple of days." You would've thought that she was an advertisement for the patch. She said, "I slept better, I—sex was better." She said, "I—my eyes weren't so dry." I mean anybody would

have loved to have her advertising for the patch. And she teaches at Loma Linda University in the Family Practice Department and she said, “Oh, I’m giving a lecture to the alumni convention.” And I said, “What’s your lecture on?” And she said, “The happy hormone.” And so she felt so strongly that she wanted to share what her experience had been.

And the only problem that I see with the generic patch, and I know that generics a lot cheaper, and if my patients can do fine on a generic and feel fine, I say go with the generic, but the problem with the generic patch is they fall off and patients tell me all the time...they’ll come in and they’ll say, “I just don’t feel as good as I did.” And I say, “Well, what changed.” And they say, “Well, the pharmacist put me on a generic.” And those are the only times I get really concerned about having a generic.

A couple of other advantages...the other advantage I think is that we have to have options and I figure the patch because I’ve seen a difference in women’s lives and I just think we do women a disservice when we don’t have some really good options.

Thanks for your time.

Dr. Sutton: I have a question for you. Are you saying, then, that the patch, from your experience, is better than the pill?

Dr. Ludders: For some women, yes. Definitely.

Dr. Sutton: It doesn’t matter whether it’s estradiol or conjugated estrogen or any of the other forms?

Dr. Ludders: You know, it seems to be very, very individually. What I’m getting is women \_\_\_\_\_ and don’t feel good and then I would try—I try everything. I tell women that a lot of medicines like, you know, like the \_\_\_\_\_ and Esclim, if what I do is like this, I’ll go like this until we get like this and you’ll know and I will know when you feel better. So, no, I would try everything, but I’ve had more consistently better luck in my women emotionally who have not done well on other things and the injection you get the bonus affect and that’s the trouble with the injection, the \_\_\_\_\_ had estradiol levels we should be between 60 and 120; it’s coming back 5,000 and 2,000 levels. What are we doing to these women’s \_\_\_\_\_. So, no, it’s very individual and I have a really good study—I can leave a lot of stuff with you—this sphere off here is talking about the brain and how we have to take \_\_\_\_\_ for brains. All the women in the HERS and the WHI, they had established atherosclerosis. We do nothing but harm for those women yet we try to extrapolate this through the perimenopausal \_\_\_\_\_.

Thank you.