Rachel Strutton-Draft

Pharmacy and Therapeutics Committee Meeting Record

Date: 1/18/08 **Time:** 9:00 a.m. – 3:45 p.m. **Location:** Idaho Medicaid, 3232 Elder Street, Conference Room D

Moderator: Don Norris, M.D.

Committee Members Present: Phil Petersen, M.D.; Thomas Rau, M.D.; Donald Norris, M.D.; Tami Eide, PharmD; Michelle Miles, PA-C; Rick Sutton, RPh; Stan Eisele, M.D; Tim Rambur, PharmD; Mark Johnston, RPh; Catherine Gundlach, PharmD

Others Present: Steve Liles, PharmD; Selma Gearhardt, PharmD; Kathy Eroschenko, PharmD; Chris Owens, PharmD; Bob Faller; Rachel Strutton

Committee Members Absent: Andrew Olnes, M.D.; William Woodhouse, M.D

AGENDA ITEMS	PRESENTER	OUTCOME/ACTIONS
CALL TO ORDER	Don Norris, M.D.	Dr. Norris called the meeting to order.
Committee Business		
➢ *Roll Call*	Don Norris, M.D.	Dr. Norris read the Roll Call
➢ *Reading of Confidentiality Statement*	Don Norris, M.D.	Dr. Norris read the Confidentiality Statement
➢ *Approval of Minutes from October 19, 2007 Meeting*	Don Norris, M.D.	There were no corrections. Minutes were approved as published.
➢ *DERP Updates*	Tami Eide, PharmD	Dr. Eide presented key questions for the following topics from the Drug Effectiveness Review Project: Second Generation Antidepressants Controller Medications for Asthma Newer Drugs for Insomnia Antiepileptic Drugs for Nonepilepsy Conditions Topical calcineurin inhibitors She also announced results of literature scans for the following drug class updates. Newer Drugs for Insomnia – Journal Article Statins – will not be updated

		Newer Antiemetics will be updated Targeted Immune Modulators – will be updated
DUR Review ➢ *Long Acting Opiods*	Chris Owens, PharmD	Long Acting Opiods Dr. Owens presented the DUR Outcome study on Long-Acting Opiods. He gave a brief background of the drugs of this class review including Morphine sulfate ER, Fentanyl, Oxycodone ER, Oxymorphone and Methadone. This review had an emphasis on methadone safety. The study demonstrated that there was a significant decrease in drug and health-related costs. There was an increased incidence of opioid poisoning and hospitalized respiratory depression in 2004 and 2005, with a decrease in 2006 following MMA implementation. Further analysis will be done on patients who received Methadone and experienced negative outcomes.

Public Comment Period

Don Norris, M.D.
Bob Faller, Medical Program Specialist

Twenty-three (23) people signed up to speak during the public comment period. Public comment was received from the following speakers:

Speaker	Representing	Agent	Class
Dr. Robert Franklin	Self	Benicar & Azor	Angiotensin Modulators -ARB
Dr. David Hinchman	Self	Benicar & Azor	Angiotensin Modulators -ARB
Dr. Sherwin Dronze	Self	Avandia	Hypoglycemics, TZD
Dr. Robert Lee	Self	Lipitor	Lipotropics, Statins
Dr. Donald Stott	Self	Lipitor	Lipotropics, Statins
Dr. Arnold Silva	Self	Tekturna	Angiotensin Modulators
Kyle Ashton	Reliant/GSK	Lovaza	Lipotropics, Others
An Phaw	Schering	Zetia/Vytorin	Lipotropics, Other
Roy Palmer	Pfizer	Atorvostatin	Lipotropics, Statins
Sue Heineman	Pfizer	Caduet	Stain/CCB Combo
Kay Leslie	Genentech	Nutropin and Nutropin AQ	Growth Hormone
Rob Meier	Pfizer	Genotropin	Growth Hormone
Contessa Fincher	EMD Serono	Saizen	Growth Hormone
Mandy Hosford	AstraZeneca	Crestor	Lipotropics, Statins
Linda Burckett	Novo Nordisk	Norditropin	Growth Hormone
Jon Beaty	ARB Boehinger	Myocardis	Angiotensin Modulators
Dan James	Bristol Myers	Avalide	Angiotensin Modulators
Cindy Giambrane	Novartis	losartan	Angiotensin

				Tekturna	Modulators
		Glen Ingrum	Merck	Cozaar & Hyzaar	Angiotensin Modulators
		Mandy Hosford	AstraZeneca	candesartan & Atacand	Angiotensin Modulators
		Rick Pham	GlaxoSmithKline	Avandia	Hypoglycemics, TZD
		Lisa Sanchez-Trask	Takeda	Actos & Amitiza	Hypolycemics, TZD & Constipation
		Diana Orentas-Lein	Santaras	Zegerid	Proton Pump Inhibitors
		Hamta Madari	DaiichiSankyo	Benicar & Azor	Angiotensin Modulators -ARB
Drug Class Review in the morning session ➢ Diabetes Combination Drugs	Kim Peterson, M.S. OHSU EPC	Diabetes Combination Drugs Ms. Peterson presented the Drug Class Review on Fixed Dose Combination Products for Diabetes that was completed in October 2007. This report sought to explore the evidence on whether fixed dosed combination products have advantages over monotherapy or co-administration in adults with Type 2 Diabetes. Compared to component monotherapies, Glucovance and Metaglip had superior HbA1C control in both first and second-line therapy. Avandamet and Avandaryl had superior control in first line therapy. Adverse events were consistent with component monotherapies . Metaglip and Avandaryl had an increased hypoglycemia increase compared to sulfonylurea monotherapy. Compared to co-administration, adherence outcomes were superior for both Glucovance and Avandamet, but it is unclear of the benefit to HbA1c Control or health outcomes. There is a lack of evidence for Actoplus Met, Duetact and Janumet.				
➢ Hyperlipidemia Combination Drugs	Marian McDonagh, PharmD OHSU EPC	Hyperlipidemia Combination Drugs Dr. McDonagh presented the Drug Class Review on Fixed Dose Combination Products for Hyperlipidemia. There were no studies comparing Advicor or Vytorin to co-administration with components. Advicor showed better LDL lowering compared to lovastatin monotherapy, but the difference was less when compared to simvastatin monotherapy and it was less effective than atorvastatin monotherapy. The addition of niacin with Advicor increased the rate of withdrawals due to flushing and related adverse events. Vytorn has evidence of statistically significant greater LDLc lowering compared to statin montherapy. There are mixed results with two studies on significant differences in Vytorin vs Atorvastatin montherapy for achievement of NCDP ATP III Goal. In one study Vytorin was superior to rosuvastatin in achieving this goal. There were mixed results on triglyceride and HDLc changes. There were not significant differences for adverse events with Vytrorin vs monotherapy. There is not evidence on				

		adherence and very little evidence looking at subgroups.
➢ Drugs for Constipation	Gerald Gartleher, M.D. OHSU EPC	<u>Drugs for Constipation</u> Dr. Gartleher shared the final report on Constipation Drugs completed in August 2007. He stated that existing evidence is poor in quantity and quality. For many of the drugs, evidence on the general efficacy is entirely missing. In conclusion, evidence is insufficient to draw conslucsions about the comparative efficacy and safety of constipation drugs.
➢ Hormone Therapy for Women in Menopausal Transition or Postmenopausal Stage	Susan Carson MHP, OHSU EPC	<u>Hormone Therapy for Women in Menopausal Transition or Postmenopausal Stage</u> Ms. Carson presented this updated drug class review. The review concluded that all of the agents had similar efficacy for reduction of hot flashes and improvement of bone mineral density. All agents had comparative incidences of adverse events. There was insufficient evidence to compare fracture prevention, long-term harms or effectiveness and safety in subgroups.
Committee Clinical Discussions and Conclusions	Don Norris, MD	<u>Diabetes Combination Drugs</u> No compelling clinical data to support any changes at this time. <u>Hyperlipidemia Combination Drugs</u> No compelling clinical data to support any changes at this time. <u>Drugs for Constipation</u> Zelnorm has been removed from the market. There is a new over the counter (OTC) preparation for Miralax. Because of prescriber concern, Medicaid is covering both the generic and the OTC preparations. Utilization review needs to be conducted for age of user before any changes. <u>Hormone Therapy for Women in Menopausal Transition or Postmenopausal Stage</u> No compelling clinical data to support any changes at this time.

Drug Class Reviews Continued Afternoon session		
➢ Angiotensin Modulators	Steve Liles, PharmD	Angiotensin Modulators (ARBs included) This is a reclassification that includes the angiotensin receptor blockers (ARBs), angiotensin cholinesterase enzyme inhibitors (ACEI), and the direct rennin inhibitor. Dr. Liles stated the ARBs were last reviewed in October of 2007 and the ACEI class was last reviewed April 2007. He shared that there is a new FDA approved indication for Valsartan for heart failure in children and adolescents ages 6-16 years. . Dr. Liles shared six (6) clinical trials including EUROPA, SMART, ADVANCE and two (2) meta-analysis, including one from AHRQ.
➢ AntiAngiotensin Modulator-Calcium Channel Blocker Combinations	Steve Liles, PharmD	AntiAngiotensin Modulator-Calcium Channel Blocker Combinations Dr. Liles stated the class was last reviewed October 2007. He shared the two (2) new drugs that have been added to this class; Exforge (valsartan/amlodipine) and Azor (olmsartan/amlodipine).
➢ Lipotropics, Other	Steve Liles, PharmD	Lipotropics, Other Dr. Liles stated the class was last reviewed October 2006. Dr. Liles shared three (3) clinical trials. He also reviewed the AHA guidelines for treatment of lipid abnormalities in children, as well as the AACE guideline update for treatment in Type 2 diabetes.
➢ Lipotropics, Statins	Steve Liles, PharmD	Lipotropics, Statins Dr. Liles stated the class was last reviewed October 2006. The new indications within this class were presented. He also reviewed three (3) clinical trials, one (1) TNT subanalysis and one (1) database analysis. These included the METEOR, CORONA and ANDROMEDA studies. Dr. Liles also shared one (1) observational study and reviewed the findings of the NLA Statin Safety Task Force as well as the AHA guidelines.
➢ Hypoglycemics, Meglitinides	Steve Liles, PharmD	Hypoglycemics, Meglitinides Dr. Liles stated the class was last reviewed October 2006 and there is no new significant information for this drug class at this time.
➢ Hypoglycemics, TZDs	Steve Liles, PharmD Steve Liles, PharmD	Hypoglycemics, TZDs Dr. Liles stated the class was last reviewed October 2006. He shared the FDA warnings, safety alerts and their advisory committee results. There are new boxed warnings for this drug class that were presented as well as the ADA/EASD updated guidelines. Dr. Liles shared five (5) clinical trials, four (4) Meta-Analysis and two (2) Cochrane reviews. Also reviewed were a systematic review and a database analysis.

➢ Proton Pump Inhibitors ➢ Ulcerative Colitis Agents ➢ Erythropoiesis Stimulating Proteins ➢ Growth Hormone Producsts	Steve Liles, PharmD Steve Liles, PharmD Steve Liles, PharmD	<u>Proton Pump Inhibitors</u> Dr. Liles stated the class was last reviewed February 2007 and there is no new significant information at this time. <u>Ulcerative Colitis Agents</u> Dr. Liles stated the class was last reviewed February 2007. He shared one (1) clinical trial. <u>Erythropoiesis Stimulating Proteins</u> Dr. Liles stated the class was last reviewed February 2007. He presented the new FDA black box warnings from March and November of 2007, as well as the recent studies submitted to the FDA. Dr. Liles also shared ASCO guideline updates. <u>Growth Hormone Products</u> Dr. Liles stated the class was last reviewed February 2007 and there is no new significant information for this drug class at this time.
Committee Clinical Discussions and Conclusions continued	Don Norris, MD	<u>Angiotensin Modulators (ARBs included)</u> No compelling clinical data to support any changes at this time. <u>AntiAngiotensin Modulator-Calcium Channel Blocker Combinations</u> No compelling clinical data to support any changes at this time. <u>Lipotropics, Other</u> No compelling clinical data to support any changes at this time. <u>Lipotropics, Statins</u> No compelling clinical data to support any changes at this time. It was noted that differences noted with atorvostatin are in the higher 80 mg dose which is not used frequently in our population. <u>Hypoglycemics, Meglitinides</u> No compelling clinical data to support any changes at this time. <u>Hypoglycemics, TZDs</u> No compelling clinical data to support any changes at this time. There is no reason to choose one agent over the another. <u>Proton Pump Inhibitors</u> No compelling clinical data to support any changes at this time. This class is still very well suited for therapeutic interchange.

		Ulcerative Colitis Agents No compelling clinical data to support any changes at this time. There might be an advantage to Lialda for convience with once a day dosing. Erythropoiesis Stimulating Proteins No compelling clinical data to support any changes at this time. Growth Hormones No compelling clinical data to support any changes at this time.
Closed Executive Session	Paul Leary, Medicaid Deputy Administrator	The Committee recommended that there be open access to Estrogens and that they be removed from the PDL. The Committee felt the Department should continue to cover generic PEG and supported the current Amitiza criteria for prior authorization.

Pharmacy and Therapeutics Committee
Public Comment
January 18, 2008

Dr. Robert Franklin
What I would like to tell you is that I would like to speak on behalf of all the ARB's. I think it's an excellent class of medications. I think all the recent studies would show that the foundation for hypertension control should be based on renin suppression, and I think responsible physicians will always use generic ACEs first, but there is a fair bit of intolerance in the ACE inhibitor, probably higher than their stated literature, which says about 10-12%. I think that the combination drugs ought to be also considered, the ARBs with the calcium channel blocker amlodipine. You essentially get the calcium channel blocker for free, which makes it a very useful medication, because then you can add on a diuretic very inexpensively, and then tolerability; I think that the drug class, the ARBs, are very well tolerated, and my clinical experience has been that they are a wonderful class of medication. Do you have any questions for me? Thank you.

Dr. David Hinchman
I'm Dave Hinchman, a cardiologist in Boise. I'd also like to ask the Committee to consider leaving on Formulary Benicar and the potent ARBs, in that I think this medication class is extremely well tolerated, very low side effect profile that allows patients to stay on the medication, and it comes in a once-a-day formula that allows for easy compliance. The ARB class in general has been favorable with cardiovascular outcomes also in preventing strokes more favorably than beta blockers, preventing the new onset of diabetes, and they are potent blood pressure lowering drugs

that are more effective than generic ACE inhibitors alone. They also do come in these fixed dose combinations with the diuretic like Benicar-HCT or with amlodipine, and studies have shown in the Kaiser database that these fixed-dose combinations allow patients to comply better with their home regimen for blood pressure control and that when they kind of run out of one agent but not another, they may not show up at the pharmacy to refill their drugs until they're out of more medicine, so combining the drugs has been shown to increase compliance with taking blood pressure medications. Any questions? Thanks.

Dr. Sherwin D'Souza

Hi, good morning. My name is Sherwin D'Souza, and I'm a practicing internist in Pocatello. I am actually here on behalf of my patients and on behalf of my colleagues that manage type 2 diabetes. I don't think I'm stretching it to say that managing type 2 diabetes is not easy. In fact, it's a challenge getting people to goal; HA1c less than 6.5 and keeping them there is a constant struggle. What I would like to ask for is basically to just leave the choices we have on board as far as TZDs go. I use both TZDs, Actos and Avandia, and I think each of them has a niche, and despite the current controversy or issue surrounding Avandia, I do believe that it's a very effective agent when used with the right patient, keeping in mind the black box labels that have been already issued by the FDA. So on behalf of my patients and my colleagues, I think it would be helpful to have the entire class left intact, so we have the choice, and are free to prescribe the drugs to keep patients at goal, which eventually basically reduces the long-term complications of diabetes. That's all I have to say. Any questions? Thank you.

Dr. Robert Lee

Hi everyone. Many of you have known me over the last several years. I've been here several times to talk on the behalf of several of the drugs, and one of my pets is probably Lipitor or atorvastatin sodium. You probably all heard some of the recent news, but one thing that I want to point out about Lipitor is that, you know, all the landmark studies recently in the recent past, within the last probably 3-5 years, all the landmark studies including PROVE-IT and REVERSAL, these are some of the trials you probably heard of, you know all these studies have been done with Lipitor or atorvastatin sodium 80 mg as the active arm. This drug has been compared against what's considered to be routine and standard therapy, which is other statins, so this drug has been compared to simvastatin 40 mg, pravastatin 40 mg, and it always has come out on top on as far as outcomes. So, you know, we know that atorvastatin 80 mg is a very beneficial drug. There have been regression analyses and meta-analyses that have compared the high-dose Lipitor to other agents, and, you know, the statement has been made in the past that all that matters is LDL reduction. Well, you know, this recent study, the ENHANCE study that you probably all heard of in the news, is the reputation of that and although this is only study and one study of about 700 patients, it definitely gives us pause. I have been saying for the last several years that we need to treat our patients based on evidence-based medicine. Evidence-based medicine at this point tells us, with our patients with hyperlipidemia, we should be treating them with a high dose of atorvastatin. The secondary end point that we've looked at is LDL reduction, and yes, all these drugs provide LDL reduction, but the most recent study, the ENHANCE study, comparing Vytorin which is simvastatin plus ezetimibe, comparing that to just plain old simvastatin came out with a negative outcome for the arm with the ezetimibe. So, you know, we wonder, you know, I've always wondered, "Well, is it the high-dose atorvastatin or is it the LDL reduction that makes my patients get better in when I use Lipitor?". Well I think that this provides a small key and the answer. So I would support that Medicaid continue to allow the use of Lipitor as far as one of its primary LDL reducing agents. Does anybody have any questions? Thank you.

Dr. Donald Stott

I'm Dr. Donald Stott, a cardiologist here, and I'm talking on behalf of atorvastatin as Dr. Lee did as well. He's pretty much covered the territory. The Vytorin issue is still up for grabs, I think, as a high-risk population of approximately 700 patients, and I'm not sure how all that gauges in on that, but atorvastatin has behind it strong evidence-based medicine. There are two really strong trials for primary prevention. They all had lipid-lowering trial which really involved hypertension in patients who had additional risk factors, and it totally reduced coronary events clearly and significantly, but another trial along the same line looked at the diabetic population, the CARDS trial. Once again, the same type of good results were obtained, and this was with 10 mg of atorvastatin, but looking at the secondary prevention list, where one investigated whether a higher dose of atorvastatin produced additional benefit, the treatment new target (this is the TNT trial, which is one of the more recent trials) compared 10 mg to 80 mg of atorvastatin, again showing an additional 20-30% reduction in coronary heart events, but one of the very interesting parts of that trial was whether it has to do with LDL lowering or some other pleiotropic effect of the drug, was the fact that congestive heart failure admissions were reduced by 26% in a whopping 41% of patients with established congestive heart failure. That was impressive enough to have the FDA allow that drug to be labeled for treatment with patients with congestive heart failure. Another trial, the ALLIANCE trial, simply looked at aggressive lipid lowering in what we would call a "real world" population of patients already well managed, who are already taking statin drugs, diet, etc., by further lowering the LDL with aggressive therapy, would that be beneficial, and once again there was an additional 20% reduction in coronary heart events. So clearly this particular medication, I admit that all the statins are valuable, but this one really carries with it, true evidence-based medicine that tells us that it should be strongly considered in its use. Thank you. Any questions? Thanks.

Dr. Arnold Silva

Good morning. I'm a nephrologist here in Boise and I would like to ask the Committee to consider the addition of Tekturna, aliskiren, which is the first and only DRI drug (direct renin inhibitor drug) for inclusion on the Formulary. One of the first questions people often ask, is "Do we need another class of antihypertensive agents?" and I think that we do. We know that when we treat patients with advanced disease, the foundation of our therapy is really using drugs that block the renin angiotensin system and we're certainly big fans in Nephrology of the ACE inhibitors and the ARBs, however we do have dose limitations with the ACE inhibitors. As you increase ACE inhibitor dosing, for example, the incidence of cough which is reported to be about 5% increases to as much as 40% or more, so we know that our patients are going to need at least a couple of drugs, and likely three or four drugs. I'm often kidded about how nephrologists use every class of drugs to try to get the patients to goal blood pressure, but indeed, I have many patients that are on five, six, and even seven, antihypertensive agents in an attempt to get them to goal blood pressure. With Tekturna, aliskiren, which is the first DRI, we've got data now on several thousand patients to show that it does lower blood pressure, it does reduce proteinuria by itself and also in combination with other agents. It's been studied in combination with an ACE inhibitor, ramipril, it's also been looked at in combination with an ARB, valsartan, with a calcium channel blocker, amlodipine, which is a popular combination these days, as well as a thiazide diuretic, and I think getting access to this class of drugs that's efficacious and has been shown already in its first year on the market to reduce proteinuria and improve that parameter which we treat often in Nephrology, I think it's a very important tool for us in Nephrology, as well as in other areas of medicine where we're trying to be aggressive with the management of hypertension. So I ask that you give it consideration. It's a highly efficacious drug and very well tolerated, which probably compares to the ARB class. Are there any questions for me?

Question from the Committee: Where do you use it in therapy? Is it a first line, second line?

Answer: It can be used as a first line therapy. It's efficacious and it typically lowers systolic blood pressure by about 15 mmHg in a patient with stage-I hypertension. It can be used in combination as well, either with a calcium channel blocker, an ACE, ARB, or a thiazide.

Kyle Ashton

Good morning. My name's Kyle Ashton and I'm from the Medical Affairs Department at Reliant JSK Pharmaceuticals, and today I'm going to highlight some key features about Lovaza, particularly its efficacy and safety. Lovaza's the first and the only prescription omega-3 fatty acid, and is FDA approved for treatment of triglyceride levels above 500 mg/dyslipidemia. Lovaza has also been shown to be effective in patients with triglycerides of 200-499 mg/dyslipidemia, and Reliant JSK has had new information placed on the label by the FDA in combination with simvastatin. The COMBOS study was designed to assess whether therapeutic doses of Lovaza could further reduce non-HDL cholesterol, triglycerides, and other lipid parameters in patients when added to stable statin therapy in hypertriglyceridemic patients who were less than 10% above their NCEP/ATP 3 LDL-C goals. COMBOS was a US based, multi-center, randomized, double-blind, placebo-controlled, parallel group study. After a diet/statin lead-in phase, subjects less than 10% above their LDL-C goals were randomized to receive open label simvastatin 40 mg, plus either double blinded Lovaza 4 gm per day or placebo during an eight-week treatment period. Lovaza 4 gm per day significantly reduced non-HDL cholesterol, triglycerides, total cholesterol, VLDL cholesterol, apo-B levels, and increased HDL cholesterol and LDL cholesterol from baseline relative to placebo. Lovaza is not indicated in patients taking statins whose triglyceride levels remain elevated. From a safety standpoint, there are no warnings on the label, Lovaza is very well tolerated, and no serious adverse events have been reported from Lovaza trials. The only statistically significant side effect relative to placebo was taste perversion to burping, and it was reported by 6 of 226 patients taking Lovaza. Drug-to-drug interactions, due to cytochrome P450 metabolism were not expected, because the drug is rapidly absorbed into cellular membranes and does not interfere with the P450 activity at the clinical dose. So in summary, Lovaza is the first and only FDA-approved Omega-3 drug indicated for treatment of patients with very high triglycerides. Lovaza has been demonstrated to be effective in monotherapy, reducing triglycerides by 45% and in combination with a statin, reducing triglycerides about 30% beyond what the statin has already done. Lastly, Lovaza is well tolerated and multiple clinical trials have demonstrated no significant adverse events, and again there are no warnings on the label. So on behalf of Reliant JSK Pharmaceuticals, I thank you for the opportunity to present today.

An Phaw

Good morning, I'm Dr. An Phaw, Medical & Science Liason in Cardiovascular with Schering-Plough and I would also like to thank the P&T Committee for the opportunity to provide public comment on the clinical benefits of Vytorin and Zetia as critical options for first line treatment for hypercholesterolemia. Before I go any further, I would like to ask you to look around this room at the three doors we have here. As you know, cholesterol comes from three sources; one is dietary, biliary source of cholesterol, and cholesterol from the liver. As you know, Zetia has a unique mechanism of action that blocks the absorption of cholesterol in the intestine, including the cholesterol both from dietary and biliary sources. Zetia is indicated as monotherapy or in combination with a statin for reduction of elevated cholesterol, both total, LDL and apolipoprotein in patients with primary hypercholesterolemia. More importantly, the results of several recently conducted Zetia clinical studies, including EXPLORER, have shown a remarkable, fabulous success in lowering LDL as much as 70% with the help of Zetia efficacy; a real hope for those tough to treat patients. Vytorin, a powerful lipid-lowering therapy is available in a once-a-day tablet. The active ingredients in this are ezetimibe and simvastatin and Zetia is the first and only first line lipid lowering agent approved to simultaneously treat these sort of cholesterols through the liver and through the intestines. Complimentary dual-acting mechanism of action reduces LDL by 52% at a usual starting dose of 10/20 mg. Furthermore, Zetia is also indicated to increase HDL and lower triglycerides. In three large, recently conducted trials, head-to-head with Crestor and Lipitor in type 2 diabetics involving an aggregate of 6,000 patients, Vytorin demonstrated superior efficacy to both Lipitor and Crestor in achieving the LDL reduction of less than 70. More importantly, several large outcomes trials involving well over 20,000 patients in aggregate are currently underway to assess the additional benefit of Vytorin on cardiovascular morbidity and mortality above and demonstrated by that of

simvastatin. Most importantly, Vytorin has not demonstrated any adverse event profile significantly greater in scope or quantity than statin alone. In summary, cardiovascular is a silent disease and chronic drug patient adherence is critically important and patients would likely adhere to medications that are simple to take and efficiently getting to goal. Therefore, I would like to thank the Committee for their consideration. I would respectfully ask the P&T Committee to place Vytorin and Zetia onto the Idaho State Preferred Drug List. Thank you.

Roy Palmer, MD

Good morning, my name is Dr. Roy Palmer. I'm a Medical Director with Pfizer and I would just like to take the opportunity to say a few words about atorvastatin. Since the last time you reviewed statins, we have had even more positive data with atorvastatin, so I just wanted to highlight kind of a big picture point of view, you know, why we have a lot of confidence in what this drug does in patients. The primary point is the outcomes data. We heard a little bit about that already. We have over 400 clinic studies we've completed with atorvastatin in over 80,000 patients and especially many of those patients with large, long-term outcome studies 3-6 years in duration for many of them, and we've covered pretty much every type of patient that is likely to be prescribed a statin in clinical practice from primary prevention, secondary prevention, people with diabetes, people with hypertension, and high risk patients as well; acute chronic syndromes and most recently patients who have already had a stroke. So, not only those low-dose studies, but we very aggressively studied the efficacy and the safety of the 80 mg highest dose available, and from a safety perspective, I think that's very important. You really don't know the safety of a drug until you've studied it in thousands of patients over many years. We've done that and we published that data. In fact, the 80 mg dose alone, we published data from over 40,000 patients. The purpose of doing that was so that you would have a great deal of confidence in what this drug is going to do in terms of outcomes, LDL reduction and imaging end points are very good. There are important intermediary steps, but ultimately what we care about is outcome, so that's the principle of evidence-based medicine. So in summary, we saw with the Enhance study this last week that until we do the trials, we really don't know what's going to happen. That's why we've done these studies, put a lot of weight behind it, and I hope that when you come to consider your preferred drug list, it stands that you once again decide to keep Lipitor on. Thank you very much.

Sue Heineman

Hi, good morning. I'm Sue Heineman, a pharmacist here in Boise and Medical Outcomes Specialist with Pfizer. Just real briefly, I wanted to talk in support of Caduet. It's a single pill combination of amlodipine and atorvastatin. You guys have heard all the positive outcomes with atorvastatin and safety. This agent, Caduet, is a single-pill combination. It supports that lack of patient adherence that we see with antihypertensive therapies with lipid-lowering therapies. In fact, the people who have both high blood pressure and lipid issues, a third of them are noncompliant after a year, and we know through published studies that say if you start both an antihypertensive agent and a lipid-lowering agent at the same time, patients are going to be more adherent. If you use a single drug combination, they will be more adherent. If you have a once-daily drug, the patient will be more adherent, and this product, a single combination of amlodipine and atorvastatin still has the cardiovascular benefits of amlodipine plus the benefits of atorvastatin all in one pill, just to support the financial outcomes for you, the efficacious outcomes for the patient, and I would respectfully ask that you reconsider this agent. I think currently it is a non preferred agent and it's not overly utilized and it's not going to be abused, and I would hope that your PA process would make the products that need to be available, available without going through any loopholes, and this is not an agent that's going to be subject to too much over use and putting a financial strain on your system. So I would just respectfully ask that you put this back on your preferred list. Thank you.

Kay Leslie

Good morning. My name is Kay Leslie and I am a Regional Clinical Endocrine Coordinator with Genentech and I'm also a registered nurse. I'm here today to discuss our growth hormone products of Nutropin and Nutropin-AQ. We have the following indications approved by the FDA: Pediatric growth hormone deficiency, chronic renal insufficiency, Turner's syndrome which is for girls, idiopathic short stature, and adult growth hormone deficiency. We also have two label extension approved by the FDA. The first one is a pubertal dosing for pediatric growth hormone patients who have reached Tanner stage 2. The second label extension is for bone mineral density dosing in childhood onset growth hormone deficiency. Nutropin-AQ is a premixed liquid version of Nutropin that is ready for immediate injection and is available in vials of 10 mg/2 ml, as well as cartridges for the Nutropin-AQ pen in the same concentration, 10 mg/2 ml in cartridges. Nutropin powdered, or the lyophilized product, comes in two strengths: 5 mg vials and 10 mg vials, and it can be customized for concentration with a mixture of the diluent as prescribed by the physician, which is actually very convenient for the family, so that you can concentrate the volume of the dose. Genentech has a personalized reimbursement support program, called The Single Point of Contact, which assists with authorizations, document submission, appeals and recertifications. They can also arrange for injection teaching for the patients in their homes or at the clinic. Stepping Stones is a Genentech compliance building program for our patients on Nutropin products, which has the nurse hotline with live professional help. It's like adding an extra nurse to the offices who prescribe Nutropin. They have tracking ability with the online program, doctor's appointments, pharmacy reorders, growth tracking, and Families For Families and much more. Just this month, the FDA approved yet another device. It is called the Y20 Nutropin-AQ pen, which contains 20 mg/2 ml, which is twice the concentration of our 10 mg/2 ml pen device, thus allowing a smaller volume for injection with another option for providers to customize treatment for their patients. For all of these reasons, I am asking you to include both Nutropin and Nutropin-AQ on your PDL for your Medicaid patients, because we are very committed to providing all of these services for your patients and for all patients with our programs to assist them in caring for their families. Thank you very much for your time today. Are there any questions? Thank you.

Rob Meier

Rob Meier, Endocrine Care Specialty here in Idaho. I speak on behalf of Genotropin. Let me just give you four key points that might be helpful in your consideration of keeping Genotropin on Formulary. First, Pfizer has a large registry for patients that enter treatment with Genotropin. This is the largest registry; 60,000 patients and over twenty years of experience. The benefit to the physician is that they can query on that registry to determine side effects and benefits based upon gender and race, so the physicians like that support that they have. In terms of the Pfizer Bridge Program, this is a patient assistance program, 24-hour support for teaching and training. We provide all the ancillary devices for the patient as well. Another thing that we will provide would be a broad range of indications for the patient, two of which Genotropin has are unique to Genotropin. Finally, our devices: we have the MiniQuick, which is the only preservative-free device, so if the patient is allergic to a preservative, they can take it without... So just respectfully ask for your consideration of maintaining Genotropin on the Formulary.

Contessa Fincher

Hello, my name is Contessa Fincher and I'm a Senior Manager of Outcomes & Market Access at EMD Serono. My professional background includes conducting outcomes research for the FDA Institute of Medicine in the pharmaceutical industry. I'm presenting on Saizen, somatotropin, to review key clinical information for your consideration and to introduce you to a new device, Easypod®. Saizen is available for a broad portfolio of growth hormone devices that suits the needs of patients from newborns to adults and is distributed in 8.8 and 5 mg vials, as well as 8.8 mg Clickeasy® cartridges. EMD Serono offers the only needle-free delivery device, Coolclick®, as well as an auto-injector pen with a hidden needle. In addition, our newest size and delivery device, easypod®, was recently approved by the FDA in October of 2007. EMD Serono

provides the device free of charge to the patient. It must be used with an 8.8 mg Saizen Clickeasy cartridge. For patients, Easypod® requires three simple steps for a daily injection: you attach the needle, you inject the site, and you detach the needle. The dose needed is programmed into the Easypod device by a health care provider for the daily dose, which means that the patient and the parent doesn't need to do that for him. For health care providers, Easypod® offers an adherence log that allows the clinician to monitor adherence to the daily injections. Easypod® also features an adjustment setting that was specifically designed for growth hormone waste to be minimized by calculating the dose that can be optimally used within each cartridge. EMD Serono sponsored a survey this past year at MAGIC Foundation Conference for ninety-seven patients. The survey reported that 63% of parents actually throw away drug if it is not a full dose left in the vial. Over time, multiple cartridges of unused milligrams of growth hormone can lead to sizeable financial burden for the payer. EMD Serono offers a patient support program called Connections For Growth. It helps patients with questions and educational training needed for the various devices and for the use of Saizen. We understand that you currently have Saizen on your PDL and we ask that you maintain this on your preferred list.

Mandy Hosford, MD

Good morning. My name is Dr. Mandy Hosford, and despite my stature, I'm actually not speaking on growth hormone modifying agents this morning. I am speaking for Crestor or rosuvastatin. I'm a representative of AstraZeneca Medical Affairs. I have actually addressed the Committee, it may be now two years ago, and our label for Crestor has changed significantly since then, so let's just do, even though I'm sure that Dr. Lyles will do this for you, a quick label update. Crestor is still indicated to substantially lower LDL, as well as raise HDL in addition to slowing the progression of atherosclerosis, so at AstraZeneca we submitted information on thousands of patients with atherosclerosis and point studies across the spectrum of the disease, and recognized substantially positive impacts of the compound on the progression of atherosclerosis across both the carotid and the coronary vascular beds. So we are now the only marketed statin that can basically redefine success to both the physician and the patient in preventing cardiovascular disease by saying that we're not only treating your numbers, but we're treating that build-up of plaque in the vasculature that is a very, very significant risk factor for cardiovascular events. So those are the things that have changed on the label. The same things on the label are very low drug-to-drug interactions. Like Pravachol, Crestor is a hydrophilic compound, very minimally metabolized, so very low clinically significant interactions with those compounds that are metabolized by 3A4 on the Cytochrome P450 system. At this point in time, there have been over eleven million prescriptions written for Crestor and that has come with an excellent safety profile like Roy Palmer suggested, at AstraZeneca we also published and took the initiative to publish a paper on 16,000 patients and the safety that we noticed with the compound across the dose range in those patients. The statin class is a very well tolerated class and does a great job at blowing the doors off of LDL and little differences with regards to raising HDL. One other thing I wanted to say was that we can accomplish these things at a very low dose in at-risk, as well as high-risk patients. For Dr. Stott's comment, our diabetic patients, we can get 90% of those patients to goal. Additionally, Dr. Stott mentioned a very significant point about Lipitor. They do have an indication for minimizing hospitalizations due to congestive heart failure. That was based on about 700 patients in their TNT trial. At AstraZeneca, we recently wrapped up a 5,000-patient study in patients with symptomatic heart failure of ischemic etiology and recognized that we also significantly reduce their entrance to the hospital for cardiovascular or heart failure causes, and also in those patients whose coronary events were heart attack or stroke, we recognized a 16% relative risk reduction in those clinical events, so we do have outcomes data and have reported out, we have outcomes data on the way in populations that obviously have not yet been studied in the statin bibliography of research, and for that reason, I will take my last 2.5 seconds to answer any questions you might have. No one likes to ask the first question, what about the second question? Thank you very much and have a great day.

Linda Burckett

Good morning. I appreciate being here. My name is Linda Burckett, the Medical Liason with Novo Nordisk in Medical Affairs and I'm here to talk about Norditropin growth hormone from Novo Nordisk. We have four clinical indications for our growth hormone product: In June of last year, we got the only indication for treatment of short stature Jeune syndrome. We also have an indication for Turner syndrome, as well as pediatric and adult growth hormone deficiency. Nutropin is available in the Nordiflex pen, it's features are that it's the only pre-mixed, pre-filled, multi-dose, disposable growth hormone delivery device with storage flexibility. It's very easy to learn, it takes just about 3-4 steps, requires no loading, no mixing or changing of cartridges in utilization. It also has storage flexibility. We have a 5 mg and a 10 mg cartridge that can be left at room temperature for up to 77° for three weeks, as well as our 15 mg cartridge, which does require refrigeration. It's very easy to teach, it's very easy for the practitioner to prescribe because the patients have many, many doses that they can use; it's one of the finest dosing increments, so it may prevent wastage. We also have a support service that can provide transition between therapies with supplemental drugs, has experience converting patients from other products; we also have training by nurses and support services for insurance authorization, as patients transition maybe out of the Medicaid system. Patient education is available in the form of videos, as well as DVDs and written materials. I would like to show you how simple it is to use. This is our device. It's a very small device. The patient just needs to put a pen needle on it, dial in their dose, take their dose, they can get rid of their needle, and put this back on the counter or in the refrigerator, and it's almost that simple to teach. Questions? Thank you very much for allowing me to be here and Norditropin added to the Idaho Medicaid would be a very beneficial move for the Medicaid population.

Jon Beaty

Good morning. My name is Jon Beaty. I'm with the Medical Affairs Department for ARB Boehinger. I appreciate the opportunity to speak to you today about Micardis, telmisartan, an angiotensin receptor blocker. It's indicated for the treatment hypertension and may be used alone or in combination with other antihypertensive agents. Micardis-HCL or telmisartan plus hydrochlorothiazide, is indicated for the treatment of hypertension and the fixed-dose combination is not indicated for initial therapy. At doses of 20, 40 or 80 mg, the antihypertensive effect of once-daily prescription of telmisartan is maintained for the full 24-hour dose interval. With both conventional blood pressure measurement and automated ambulatory blood pressure monitoring, the 24-hour trough to peak ratio for 40 and 80 mg telmisartan is 70-100% systolic and diastolic blood pressure. This meets the FDA trough to peak recommendation for once daily dosing. The antihypertensive efficacy for telmisartan and telmisartan-HCL has been evaluated in a number of trials. In one such trial, it was evaluated in a respective randomized placebo-controlled study of 1,066 patients with stage-1 or -2 hypertension, comparing the 80 mg of telmisartan and 160 mg of valsartan, given this mode of therapy for two weeks followed by the addition of 25 mg of hydrochlorothiazide to each arm. Mean production to the baseline was seen with trough measurements were determined at the end of an eight-week treatment period, both systolic and diastolic mean trough values were significantly lower in the telmisartan-treated subjects than those treated with valsartan. There are a number of other trials that have demonstrated similar degrees of efficacy for the drug in the broad variety of patients, including those who have type 2 diabetes or chronic kidney disease as underlying conditions. Through all of those cases, efficacy is demonstrated and without further deterioration of the underlying disease. Some notes about taking telmisartan: it's very well tolerated, there is, in the label, an FDA mandated black box warning about use of the drug in the second and third trimesters of pregnancy. Thiazides cross the placental barrier and appear in cord blood and created a risk of neonatal jaundice, thrombocytopenia and possibly other adverse reactions that have occurred in adults. The safety and efficacy in pediatric patients hasn't been established. I appreciate the opportunity to speak to you this morning. If you have any questions, please ask me, and we urge you to continue including telmisartan and telmisartan-HCL as preferred on your PDL. Thank you very much.

Dan James

Good morning. I'm from the Medical Department of Bristol Myers. I just wanted to provide a very brief update to the ARB document. Just this month, the FDA granted Avalide, which is irbesartan and hydrochlorothiazide a new indication. Two trials were done in about 1,200 patients with moderate and severe hypertension. As a result of those two trials, the FDA has granted Avalide an indication as an initial therapy for patients with all stages of hypertension. Thank you.

Cindy Giambrane

Good morning. My name is Cindy Giambrane and I'm a pharmacist with Novartis Pharmaceuticals. I am here today to talk to you about aliskiren or Tekturna. Aliskiren is an orally active, non-peptide direct renin inhibitor that decreases plasma renin activity, inhibits the conversion of angiotensinogen angiotensin I. In addition, aliskiren decreases levels of angiotensin II, which is a powerful vasoconstrictor that contributes to increases in blood pressure. Tekturna is indicated for the treatment of hypertension and it can be used alone or in combination with other antihypertensive therapies. With the respect to monotherapy, Tekturna has been studied in more than six different double blind placebo-controlled eight-week trials and the studies include over 2,700 patients that have received Tekturna and 1,200 patients given the placebo. Up to 90% of the blood pressure effect is noted in the first two weeks of therapy and after cessation of therapy, blood pressure gradually returns to baseline levels over a period of several weeks. There is no evidence of any rebound hypertension after abrupt cessation of therapy. We also have a number of different studies with Tekturna in combinations, such as hydrochlorothiazide, as well as combinations with valsartan. In terms of safety and tolerability, the drug has been studied in over 6,400 patients. In terms of safety in placebo-controlled clinical trials, discontinuation of therapy due to adverse clinical event, including uncontrolled hypertension, occurred in 2.2% of patients on Tekturna versus 3.5% given placebo. It's a medication that's given once a day at 150 mg and in patients whose blood pressure is not controlled, you can increase the dose to 300 mg. Please consult the prescribing information for more details. Thank you very much for your consideration today. Thank you.

Glen Ingrum

Thank you. I'm Glen Ingrum. I'm a cardiovascular speciality representative with Merk and I know you guys have a lot on your plate today, so again thank you for your time. I'm here to talk about a product that's already on your PDL and we certainly hope and recommend it remain. That is Cozaar and Hyzaar, losartan and losartan/hydrochlorothiazide. A couple of reminders for you: You guys probably recall this from when you had Dr. Bob Aldrea here with Medical Services from Merk, and that gets us back to our outcomes data. That reminder would be around our LIFE trial, and that was the losartan intervention for end point reduction in hypertension. This was in Lancet of 2002, and the two points I wanted to remind you on: This was nearly 90-100 patients with hypertension and documented LVH or left ventricular hypertrophy, and the primary end points that came out of this landmark trial were looking at the occurrence of cardiovascular death, non fatal stroke, or non fatal MI. They compared Cozaar 50 mg and started out with Cozaar 50 mg versus atenolol 50 mg, so it's an active comparator, which is very significant when you consider the data. Systolic blood pressure reductions were reduced just over 33 mmHg and 29 mmHg for the atenolol group, and on the diastolic, it was around 16.5 mmHg. So they did achieve what they were trying to do, that was equal blood pressure lowering in both arms, but it was in the Cozaar arm that we received our primary end point reduction of 13%, as well as a 25% reduction in stroke, so again very significant when you look at the active comparator of Cozaar and atenolol. So that was our LIFE trial. The other part of that was there was a sub-group of patients who had diabetes. You heard from the other physicians who were here talking earlier around the importance of stroke and diabetes, and what a detrimental effect it would have on anyone's life, but there was a sub-group in LIFE trial of nearly 1,200 patients, and 13% in this trial had diabetes at study entry, and they also saw their CV death, MI, and stroke reduced by 24% versus atenolol, so we had all parameters covered in that trial. The other reminder, a couple of quick points for you here around reen Al and that was from the New England Journal of Medicine in September of 2001, and this is where they compared 1,513 patients, Cozaar versus placebo, and the primary end point was for the first occurrence

of any of the following events: doubling of serum creatinine, end-stage renal disease, or dialysis, and what they found out in this trial was that there was a 16% risk reduction in this primary end point and the occurrence of reducing the doubling serum creatinine was by 25%. But the bottom line in this that I think a lot of our specialists really appreciate was that there was a 29% reduction in end-stage renal disease. So thank you for your time, and I will mention this real quickly because we had some specialists asking, as the first ARB on the market, we will be the first to come off expiry, which is around April of 2010.

Mandy Hosford

I'm back and it is timely, because this is sort of a surprise to you, so this is for candesartan Atacand. Real quickly, all the ARBs indicated for hypertension as you know, not all of them are indicated to reduce cardiovascular mortality and heart failure hospitalizations, as is Atacand, and it has shown that benefit either on top of an optimized dose of ACE inhibitor or in patients that are ACE intolerant, but also shows that benefit in patients with or without history of heart attack, and it also shows that benefit with once daily dosing. So that, again, just to kind of remind us, not necessarily for hypertension here, although it is indicated for that, in a heart failure population, Atacand has a very special place. So thank you again for letting me come back and I'll leave it at that.

Rick Pham

Good morning. My name's Rick Pham and I'm the Regional Medical Scientist for GlaxoSmithKline. I'm here to talk about Avandia this morning. As you know, type 2 diabetes is the leading cause of baby and premature mortality because of the microvascular complications of the disease, and glycemic control remains the cornerstone of treatment. With current guidelines endorsing more rigorous lowering of glycemic targets and early combination therapy, Avandia has actually been proven to be superior in glycemic control in our ADOPT Trial, which was a head-to-head trial against metformin and glyburide, where Avandia showed glycemic durability out to almost five years on initial line therapy compared to less than four with metformin and less than three with glyburide. Recently, a box warning for the TZD class was required for both TZDs, warning against initiating therapy in New York Heart Association class-III and -IV heart failure patients. Avandia also received a box warning addressing the FDA's meta-analysis of 42 studies with a mean duration of six months showing an increased risk of myocardiac ischemic events when compared to placebo, but not compared to active comparators, i.e. metformin, sulfonylureas and insulin. The box warning also states that three other studies with a mean duration of 41 months, however, did not confirm this risk and that the data being reviewed by the FDA in its entirety is inconclusive. Currently, there are four large outcomes trials involving Avandia; the RECORD study, the ACCORD, BARI-2D and the VA Diabetes Trial. Within these four studies, there are more than 18,000 patients enrolled, and the Data Safety Monitoring Board of each of these trials have not incurred any safety issue within these trials, and they have confirmed continuation of these trials to conclusion, which should be towards the end of this year and in 2009. Also, three US managed care database studies that contain over 1.3 million diabetic lives, also showed no increased risk with Avandia versus metformin, sulfonylurea, insulin or Actos and, in fact, two independent database analyses by Wellpoint and the Department of Defense also confirm that there was no increased risk by patients taking Avandia versus the other oral agents. So, Avandia is actually the most widely studied diabetes medication on the market today and yields safety and efficacy when used appropriately to treat patients who are not controlled with their HA1c, and it has been proven to be an effective and safe option for patients, so I respectfully request that Avandia remain on the Formulary for the Idaho Medicaid with no changes.

Lisa Sanchez-Trask, MD

Good morning. I'm Dr. Lisa Sanchez-Trask, and I'm a Clinical and Outcomes Manager for Takeda Pharmaceuticals, and I'm actually scheduled to report on two (2) different agents; Actos a TZD and also Amatiza for chronic idiopathic constipation. So in the interest of time, I'm going to start with Actos and I'll do a brief update, and if there's time, then I'll address Amatiza briefly if you'd like me to. For patients with type 2 diabetes, the Actos or pioglitazone family of products provides several convenient options for TZD mono, as well as combination therapy. I would like to just review the cardiovascular safety profile of Actos and our new changes to our label since February. Safety data from the large perspective double-blind clinical trial, PROactive, was actually incorporated in the adverse event and warning section of the Actos PI in February of 2007. The overall safety and tolerability of pioglitazone in PROactive was consistent with known adverse events. Compared with placebo, slightly more patients on the Actos group were hospitalized with heart failure, 4% versus 6% respectively, and the instance of death subsequent to a report of serious heart failure was 1.5 and 1.4 for Actos versus placebo respectively. Although there were no significant differences between Actos and placebo where the three-year incident of a first event within the primary composite end point, there was no increase in mortality or total macrovascular events with Actos, including heart attacks and stroke. In addition to this PROactive study, there are a number of meta-analyses, as well as a retrospective cohort study that has demonstrated that Actos does not increase total macrovascular events or mortality. For example, in one of the meta-analyses that represented over 16,000 patients, authors concluded that pioglitazone was associated with an 18% lower risk of death, stroke and MI. Overall, the data from the three separate analyses is consistent with, and supports, the Actos label that states that "There was no increase in mortality or total macrovascular events with Actos". In August of 2007, a black box warning was added to the PI of Actos and its combination product regarding CHF and not ischemic events. This warning places important information from the previous label in a more prominent position and provides that initiation of Actos is contraindicated in patients with New York Heart Association class-III and -IV heart failure, and additionally Actos has no warnings for use with nitrates or for use with insulin. Increased risk of fracture in female patients receiving Actos has been observed in clinical trials and was added to our label in September, so the risk of fracture should be considered in the care of female patients treated with Actos, and attention should be given to assessing and maintaining bone health according to current standards of care. Thank you for your time and your consideration of Actos. Would you like me to briefly touch on Amatiza?

Committee Answer: If you can do it in a minute and a half.

I will do my best. Amitiza, or lubiprostone, is FDA approved for the treatment of chronic, idiopathic constipation in adults, including those over the age of 65. It's a locally acting chloride channel-2 activator that enhances chloride rich intestinal fluid secretion without altering sodium and potassium concentrations in the serum. By increasing intestinal fluid secretion, lubiprostone increases motility in the intestine, which in turn increases the passage of stool and alleviates the symptoms associated with constipation. Two double-blind, placebo controlled studies in over 450 patients demonstrated that patients treated with Amitiza 24 µg twice daily had a higher frequency of spontaneous bowel movements, or SBMs. In fact, approximately 60% experienced an SBM within the first twenty-four hours of therapy and 80% experienced an SBM within the first forty-eight hours of therapy compared to placebo. In terms of the signs and symptoms related to constipation, like abdominal bloating and discomfort, these were also improved in Amitiza versus placebo-treated patients. The effects were consistent across race, gender, and in the elderly. In addition withdrawal of Amitiza following four weeks of treatment did not result in rebound effect. Lastly, in terms of its Adverse Event Profile, nausea, diarrhea and headache are the three primary adverse events and the dosing is 24 µg b.i.d. p.o. with food. So, thank you for your consideration of both Actos and Amitiza. Any questions on either of those? Thank you.

Diana Orentas-Lein

Good morning. Now for something completely different. My name is Diana Orentas-Lein, and I'm a Scientific Affairs Liaison for Santaras, and I wanted to thank you for the opportunity to present information today about Santaras's product, Zegerid, which is an immediate-release formulation of omeprazole with sodium bicarbonate. This combination product is now available in a capsule, as well as a powder for oral suspension. So you all know that PPIs are acid labile, they need to be protected from gastric acidity, and that's why all of the other orally available PPIs are enterically coated, and that's to protect the pro-drug from being degraded in the stomach and delay its release until it's in the lumen of the small bowel. Zegerid utilizes an antacid buffer sodium bicarbonate, which is administered to gather with the PPI micronized omeprazole, and this allows for immediate neutralization of the gastric acidity. It protects the pro-drug, but it also allows for a more rapid absorption profile, so you have peak plasma levels occurring within thirty minutes and in the review of this data, from the onset, the FDA has now classified Zegerid as the only PPI in immediate-release category. For that reason, it is not yet rated with any of the other omeprazole products. The pharmacokinetic differences actually translate into pharmacodynamic superior pH control. In two head-to-head published studies, Zegerid administered prior to bedtime performed higher levels of gastric pH control when compared to Protonix administered prior to dinner, or when compared to lansoprazole or esomeprazole when administered prior to bedtime. In addition, the pharmacodynamic studies that were registered with the FDA for Zegerid indicate that when 40 mg of Zegerid is administered prior to breakfast in the morning, it raises gastric pH over 4, which is the benchmark that you want, because the number of hours your pH is over 4 is correlated to healing an erosive disease, so it does this for 18.6 hours and this is higher than any of the other labels available. Additionally, there is a study that was published in The Journal of Critical Care Medicine in which the powder for oral suspension was administered through the NG tube, 40 mg, to critically ill patients, and in this study, there was a sustained and consistent pH control, so that the median gastric pH was over 6 on all fourteen trial days, and for that reason when that data was filed with the FDA, Zegerid received the indication for the risk of upper GI bleeding in the critically ill patient. It's the only PPI with this indication. So, in addition to that indication, it's also indicated in duodenal ulcer, symptomatic GERD, erosive esophagitis, maintenance and healing of erosive esophagitis, as well as treatment of active, benign gastric ulcers. I know you're short on time, but I would be happy to answer any questions.

Hamta Madari

Hello, my name is Dr. Hamta Madari. I am a Medical Liason with DaiichiSankyo based in San Francisco, California, and I'm here to testify on behalf of Benicar and Azor. Starting with Benicar, Benicar is a once-daily angiotensin 2 receptor blocker, indicated for the treatment of hypertension. Benicar can be used as first line therapy, either alone or in combination with other antihypertensive agents. An integrated analysis of seven clinical trials and approximately 2,600 patients with stage-II hypertension showed that Benicar 20 mg and 40 mg per day induced significant reductions in mean blood pressure of approximately 15/12 and 17/13 mmHg. In clinical trials, the withdrawal rates due to adverse events and the incidents of adverse events with Benicar was similar to placebo. The only adverse event that occurred in greater than 1% of patients treated with Benicar compared to placebo was dizziness. Benicar is also available in combination with hydrochlorothiazide, known as Benicar-HCT. I ask that you please maintain the preferred status of Benicar.

Azor is a new, fixed dose combination of amlodipine and omesartan. It is indicated for the treatment of hypertension alone or with other antihypertensive agents, but is not indicated for initial therapy of hypertension. An eight-week, multi-centered, randomized, double-blind, placebo-controlled trial was designed to assess the efficacy and safety of co-administration of amlodipine plus omesartan in adult patients with mild to severe hypertension in comparison to respective monotherapies. The results show that each combination therapy had significant greater reductions in diastolic and systolic blood pressure compared to both of its monotherapy components. Each active treatment group had a statistically significant mean reduction. Overall, the greatest reductions occurred in the group treated without amlodipine 10 mg and omesartan 40 mg, 30/19 mmHg reduction, followed by the group treated with amlodipine 10 mg and omesartan 20 mg at 29/17 mmHg reduction. Azor allowed

more patients to reach their respective JNC 7 goals (35-53%) as compared to the respective monotherapies (20-36%). As far as safety, the overall incidents of adverse reactions on therapy with Azor was similar to that seen with the corresponding doses of the individual components of Azor and to placebo. Edema was the most common drug-related treatment adverse effect, and was experienced by a total of 277 or 14.3% of the patients. Edema was proactively assessed and as a result, the observances were higher than reported in the package insert for either amlodipine or Benicar. I ask that you please allow patients access to Azor by considering it for preferred status.