

**ALASKA MEDICAID  
PHARMACY AND THERAPEUTICS COMMITTEE**

**Location of Meeting  
Frontier Building, 3601 C Street, Room 890/896**

**FINAL MINUTES OF MEETING  
January 21, 2011  
8:00 a.m.**

**Committee Members Present:**

Dharna Begich, Pharm.D.  
Marvin Bergeson, MD  
Amber L. Briggs, Pharm.D.  
Richard Brodsky, MD, Chair  
Robert H. Carlson, MD (telephonic)  
Jeffrey G. Demain, MD  
Vincent Greear, R.Ph.  
Daniel P. Kiley, DDS MPH  
William McCormick, Pharm D.  
John E. Pappenheim, MD  
Claudia Phillips, MD  
Jill Reid, R.Ph. (telephonic)  
Janice Stables, MSN, ANP  
Trish White, R.Ph. (telephonic)

**Committee Members Absent:**

Diane Liljegren, MD  
Andrew Maciejewski, MD  
Paul Michaud, Pharm.D.  
Sherrie D. Richey, MD

**Others Present:**

David Campana, R.Ph.  
Alex Malter, MD MPH  
Chad Hope, Pharm.D.  
Julie A. Pritchard, Pharm.D.  
Flora Solomon

**1. Call to Order – Chair**

Chair Brodsky called the meeting to order at 8:00 a.m. William McCormick was welcomed as a new committee member.

**2. Roll Call**

A quorum was present.

**3. Public Comments**

**DR. J. ROSS TANNER:** A physician at the Diabetes and Lipid Clinic of Alaska discussed TZDs. Last September, we received a letter stating patients could no longer readily be prescribed Avandia due to recent cardiovascular safety data. However, patients can receive Avandia under restricted access. TZDs are not as commonly used as they were several years ago. The majority of treatment algorithms by third-party insurers or the ADA does not mention Rosiglitazone as an option. Whenever TZDs are mentioned, Pioglitazone is uniformly accepted as being the one to use. It would be going against the

standard of practice to consider using Avandia, which is no longer available in other countries and is on restricted access by the FDA.

**DR. PATRICK NOLAN:** An endocrinologist agreed with Dr. Tanner about TZDs. Rosiglitazone has been completely removed from the market in Europe. It is difficult to get patients to take Avandia, because they see so many restrictions on it when they review the written materials. Several trials and their outcomes were mentioned. I would encourage using the TZD of choice if possible. Pioglitazone is the preferred drug in most U.S. clinics based on large amounts of data. TZDs are not all the same and Pioglitazone should be available on the PDL. I would also encourage the availability of U-500 insulin and both of the GOP analogs on the PDL.

In response to Dr. Demain, Dr. Nolan did not feel it would be challenging to switch patients from Avandia to Actos.

**DR. JOHN C. BOSTON:** Concurred with Dr. Tanner and Dr. Nolan regarding the use of Avandia. Switching patients from Avandia to Actos is a non-issue. There has been a lot of press about Avandia and I have had agents approach my clinic about discontinuing the medication, so seeing it as a primary medication on the PDL is disconcerting. In addition, patients being admitting into the hospital are switched to the hospital's formulary, which does not include Avandia. I am also concerned about the 15-milligram dosage limitation.

**DR. SAMUEL ABBATE:** An endocrinologist from Wasilla discussed U-500 insulin. We have increasing issues with obesity, particularly morbid obesity in the diabetic population. It is difficult when patients have to take large doses of short-acting insulin. The literature shows that a more concentrated form provides better glucose lowering. Although there is probably a price advantage to sticking with one manufacturer, Lilly is the only one who makes U-500 insulin. Another product is 50/50 insulin. The 70/30 insulin, which is traditionally available, traces back to the old days where it was standard to dose insulin in two-thirds, one-third, hence the 70/30. While this is effective in many patients, many other patients need a greater percentage of insulin pre-meal. The 50/50 can be very useful, particularly in the elderly or people who have difficulty calculating carbohydrate ratios and doses.

#### **4. Review of Other Acne Agents-Dapsone (Red Category)**

There were no public testimonies.

Dr. Pritchard gave the Magellen presentation on Other Acne Agents-Dapsone. Aczone, or Dapsone 5 percent topical gel, is indicated for the treatment of acne vulgaris. Topical retinoid is still the preferred primary treatment option. For inflammatory lesions, an antibiotic can be added for synergy and faster clearing. Bear in mind that antibiotics, as monotherapy or used long-term in combination therapy, is not recommended due to development of bacterial resistance concerns. Dapsone's exact mechanism of action is unknown, but it is thought to work via suppression of neutrophil recruitment oxidation, which may help prevent the production of toxic respiratory and secretory products. It may also have antimicrobial activity. Topical Dapsone has not been shown to cause peripheral neuropathy or skin reaction as reported with oral formulations, but there is some concern about mild hemolysis in patients with glucose-6-phosphate dehydrogenase deficiency. The 5 percent gel is applied twice daily to affected areas. Contact with mucus membranes, eye areas and lips should be avoided. Also avoid fire,

flame and smoking following use as the gel products are flammable. In December, there were seven claims for Aczone. The committee has not previously discussed this drug and there were no expert opinions provided.

**DR. DEMAIN MOVED A CLASS EFFECT. SECONDED BY DR. BRIGGS. THE MOTION PASSED UNANIMOUSLY.**

**5. Re-Review of GLP-1 Receptor Agonists (Red Category)**

**TODD PAULSON:** A representative of Nova Nordisk discussed Victoza. Victoza is a GLP-1 agonist. It has 97 percent amino acid homology to endogenous human GLP-1. GLP-1 is the gut hormone that stimulates insulin release in response to meals. It is glucose dependent so it works when glucoses are elevated, but it does not work when they are normal or low. Victoza is an injection, once daily indicated for type II diabetes as adjunct to diet and exercise. Modifications of this product gives it the ability to be dosed once daily, any time of the day, regardless of meals, and its dosage time and sites can be rotated. Because it is homologically human GLP-1, DPP-4 and other enzymes degrade it systemically so there is no renal or hepatic elimination and there is no dosing restrictions in patients with renal or hepatic insufficiency. Several studies and their outcomes were reviewed. The package insert, which was updated in December, was reviewed. Victoza is contraindicated in patients with a personal or family history of medullary thyroid carcinoma or in patients with Multiple Endocrine Neoplasia syndrome type 2. Victoza is indicated for monotherapy or combination therapy. According to the package insert, it is not recommended as the first line agent. Metformin should always be your first choice, and Victoza can be added. If the patient cannot tolerate Metformin, Victoza can be used as a single agent.

**JESS HONG:** A representative of Amylin made himself available to answer questions regarding Byetta. A full presentation was made last year. In the past six years, more than a million patients have been prescribed Byetta. Data comparing Byetta with many of the other products in the marketplace are available. We would ask that Byetta be retained on the PDL.

Dr. Pritchard gave the Magellen presentation GLP-1 Receptor Agonists. Exenatide (Byetta) and Liraglutide (Victoza) are used as an adjunct to diet and exercise in adults with type II diabetes mellitus. Byetta is used for patients on oral anti-hyperglycemic. Neither has been studied in conjunction with insulin or in patients with a history of pancreatitis. The incretin hormones glucagon-like peptide is part of the system involved in the regulation of glucose homeostasis. Incretins are released by the intestines throughout the day, with more being released in response to food. When blood glucose levels are normal or elevated, the GLP-1 increases insulin synthesis and releases from pancreatic beta cells while lowering glucagon secretion from the alpha cells. Together, this reduces hepatic glucose production. The GLP-1 agents were associated with a 0.5 to a 1.1 reduction in HBA1C levels and a decrease in weight of up to two kilograms from baseline as opposed to weight gain in patients taking placebo. These agents should not be used in patients with type I diabetes. In December, there were 17 claims for Victoza and 12 claims for Byetta. At the last review, a motion declaring the drugs in this class as therapeutic alternatives passed unanimously. Significant changes include Victoza became available and has the 95 percent amino acid homology to endogenous human GLP-1. It is contraindicated in patients with a personal or family history of medullary thyroid carcinoma or Multiple Endocrine Neoplasia syndrome type II. Byetta has been associated with acute pancreatitis. If pancreatitis is suspected, stop the drug immediately. Do not use in patients with severe renal impairment, end stage

renal disease, kidney transplants or gastro paresis. Byetta has been reported to raise INR in patients taking Warfarin. Both drugs slow gastric emptying, which affects the absorption of oily administered drugs, so oral medications should be used an hour before injecting.

**DR. BERGESON MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY DR. PHILLIPS. THE MOTION PASSED UNANIMOUSLY.**

#### **6. Re-Review of Immunosuppressants (Red Category)**

**GILDA HARRISON:** A representative of Astellas discussed Prograf. Prograf is indicated for the prophylaxis or organ rejection in patients receiving allergenic liver, kidney and heart transplants. It is the most widely utilized calcineurin inhibitor on the market. The clinical efficacy and safety of Prograf has been studied in over 1,400 articles, which are available upon request. Prograf also falls into the category of narrow therapeutic index medications or critical dose drugs. The characteristics of NTI medications were reviewed. Astellas submitted a citizens' petition to the FDA last year asking them to require physician/patient consultations before switching formulations, and that generic formulations of immunosuppressant drugs having a NTI be tested for bioequivalence not only in healthy volunteers, but also in transplant patients. While the FDA did not determine whether Tacrolimus was a drug with a NTI, it did conclude that standard bioequivalence standards are appropriate for Tacrolimus and approved a generic formulation in August 2009. Since then, three other generic Tacrolimus drugs have been approved. The FDA decided not to require labeling changes that would require a physician/patient consultation before formulation substitution. Physicians should have open access to Prograf if they determine it is the right drug for their patient. As a nurse who has taken care of thousands of transplant patients over the last 20 years, I know that patients do not want to have their drugs changed if their organs are working properly.

Dr. Pritchard gave the Magellen presentation on Immunosuppressants. Although there are no published guidelines in the U.S., and drugs and dosing varies, there is a general schedule for use. Induction therapy is started at time of surgery then combinations of anti-proliferative agents and calcineurin inhibitors are added. Sirolimus and Everolimus are also proliferation inhibitors, but with different mechanisms of action than Mycophenolate. Although Azathioprine has an indication for rheumatoid arthritis, it is as a last string player for that indication. Cyclosporine has indication plaque psoriasis, but it also should be used for patients who have failed standard therapies. Cyclosporine and Mycophenolate are available as different salts, but the products are not interchangeable. Everolimus, Mycophenolate and Sirolimus should not be crushed, chewed, or cut. Mycophenolate capsules should not be opened. Cyclosporine solution can be diluted with milk, apple juice or orange juice at room temperature. In December, there were 119 claims: Azathioprine, 28%; Mycophenolate Mofetil, 19%, Prograf, 12%; Tacrolimus, 11%; Gengraf, 10%; and the rest were single digit claims. At the last review, a motion to declare the drugs in the class as therapeutic alternatives passed unanimously. Significant changes include Zortress (Everolimus) was approved as adjunctive therapy in combination with Simulet for kidney transplants. Everolimus works by inhibiting protein synthesis and has no effect on calcineurin activity. This agent does have a black box warning for increased incidence of kidney graft thrombosis and has a recommendation for lowering doses of Cyclosporine when the two are used together. For patients with hepatic impairment, the dose should be cut in half. Zortress participates in REMS.

Dr. Demain said some of the drugs in this class were used off label. Physicians use Cyclosporine or Azathioprine for severe atopic dermatitis or chronic Urticaria.

**MR. GREEAR MOVED THE DRUGS IN THIS CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY UNIDENTIFIED MALE.**

Dr. Demain suggested including Cyclosporine and Azathioprine in the motion due to their frequency of use, as well as their uses outside of transplants. Mr. Campana said Cyclosporine was currently on the PDL and there was a good chance it would remain there.

**THE MOTION PASSED WITH ONE OPPOSED.**

**7. Review of Topical NSAIDS (Red Category)**

There were no public testimonies.

Dr. Pritchard gave the Magellen presentation on Topical NSAIDS. NSAIDS are used to treat osteoarthritis pain as well as other mild to moderate pains of various etiologies. Topical NSAIDS offer an alternative to oral agents for those at high risk of gastrointestinal events or those unable to take oral formulations. The elimination half-life for topical Diclofenac is about 12 hours. It is metabolized through glucuronidation and eliminated through subsequent urinary and biliary excretion. Diclofenac topical formulation should not be used in patients with asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDS. These drugs are pregnancy category C and have a similar drug and reaction profile as other NSAIDS. Hands should always be washed after applying these agents. In December, there were 46 claims: (indiscernible -- telephone malfunction) Pennsaid, 2%. At the last review, a motion for class effect, including one gel and one patch, failed. Then a motion for class effect passed unanimously. The significant changes include Pennsaid became available for the treatment of osteoarthritis of the knee. It is a 1.5 percent topical solution with about one-third the systemic exposure compared to Voltaren Gel. It is applied by placing 40 drops per effected knee, spread evenly around the area, four times a day. The most common side effect noted was dry skin. A medication guide is dispensed with Pennsaid.

**DR. BRIGGS MOVED A CLASS EFFECT. SECONDED BY MS. STABLES. THE MOTION PASSED UNANIMOUSLY.**

**8. Re-Review of Angiotensin II Receptor Blockers ARBs (Blue Category)**

Dr. Pritchard gave the Magellen presentation on Angiotensin II Receptor Blockers (ARBs). The angiotensin II receptor blockers can be used as first line anti-hypertensives. They are also acceptable alternatives to ACE inhibitors for congestive heart failure. The 2010 American Diabetes Association also suggests all diabetics be on an ACE or ARB for treatment of hypertension and to slow the progression of diabetic nephropathy. ARBs block the vasoconstrictive and aldosterone-secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT-1 receptors in certain tissues. All ARBs reduce blood pressure to a similar degree. In December, there were a total of 818 claims. Of the plain ARBS, there was 620 claims: Diovan, 33%; Losartan Potassium, 27%; Avapro, 15%; Micardis, 10%; Benicar, 10%; Atacand, 1.9%; and the remaining for Cozaar and Teveten. Of the ARB and diuretic combinations, there were 198 claims: Diovan HCT, 60%; Benicar

HCT, 13%; Losartin hydrochlorothiazide combination, 10%; Avalide and Micardis HCT, 7% each; the others were single digit or zero claims. At the last review, a motion for class effect passed unanimously. The significant changes include a meta analysis suggesting ARBs are associated with new cancer diagnosis. Candesartan (Atacand) is indicated for the treatment of hypertension in pediatrics ages 1 to 17. Losartan, Olmesartan, and Valsartan can be used in pediatrics ages 6 to 16. Micardis 80-milligram tablets are indicated for patients 55 years and older at high risk for developing major cardiovascular events and who are unable to take an ACE.

In response to Dr. Demain, Dr. Pritchard said the meta analysis suggested that all of the drugs in this class were associated with new cancer diagnosis, but did not include any specific information.

**DR. PHILLIPS MOVED A CLASS EFFECT. SECONDED BY MS. STABLES. THE MOTION PASSED UNANIMOUSLY.**

#### **9. Re-review of DPP-4 Inhibitors (Blue Category)**

**DOUG GELOWITZ:** A representative of Bristol-Myers Squibb discussed a new product, Kombiglyze XR. It is a combination of Saxagliptin and Metformin hydrochloric acid extended release. It is the first fixed-dose combination to be a once daily pill, as opposed to Janumet twice daily. As with any drug that contains Metformin, renal implications exist. The way Kombiglyze is manufactured, which keeps the pill size about the same as Metformin, was described. Kombiglyze is a once daily tablet that provides excellent control of FPG and PPG over a 24-hour period. The dosing regimen was reviewed.

**ESTHER ESTES:** A representative of Merck provided an update on Januvia and Janumet. An October 2010 clinical trial and its outcome was reviewed. In Section 6.2, we have included constipation, vomiting, and headache in the post marketing experience. Because these events are reported voluntarily from a population of uncertain size, it is generally not possible to reliably establish a frequency or a causal relationship to the use of Januvia or Janumet. Januvia and Janumet are the first DPP-4 inhibitors in the U.S. and now have more than four years of experience since its launch with 20 million prescriptions. This is the most widely studied DPP-4. The extensive efficacy data has been presented in the past. Both drugs have been demonstrated to be safe and tolerable. We ask that Januvia and Janumet be retained on the PDL.

Dr. Pritchard read a letter supporting the retention of Januvia and Janumet on the PDL from Dr. Robert Scala.

Dr. Pritchard gave the Magellen presentation on DPP-4 Inhibitors. DPP-4 inhibitor drugs can be monotherapy or used in combination with other anti-hyperglycemics. They work by inhibiting the DPP-4 enzymes in activation of GLP-1 and GIP, which prolongs the action of the incretins. By doing this, there is an increase in insulin secretion and a reduction of glucagon secretion, thereby lowering glucose levels. These agents should not be used in patients with type I diabetes. In December, there were 139 claims: Januvia, 77%; Janumet, 15%; and Onglyza, 8%. At the last review, a motion declaring the drugs in the class as therapeutic alternatives, including at least one from each sub class, passed unanimously. Significant changes include Kombiglyze XR was added to the marketplace. Kombiglyze and Janumet both carry warnings of lactic acidosis due to the Metformin component. If acidosis is suspected, discontinue drug and hospitalize the patient. There have been reports of acute pancreatitis with Januvia and Janumet. Physicians are to monitor the patient and discontinue the drugs

if pancreatitis is suspected. Januvia and Janumet dosage adjustments should be made for patients with moderate to severe renal insufficiency.

**DR. BRIGGS MOVED A CLASS EFFECT. SECONDED BY DR. PHILLIPS. THE MOTION PASSED UNANIMOUSLY.**

#### **10. Re-Review of TZDs (Blue Category)**

**LONG WIN:** A representative of GlaxoSmithKline clarified the FDA announcement made on September 23 regarding Avandia. The FDA announced that Avandia should remain on the market, but with restricted access through the administration of the REMS program, also known as the Risk Evaluation and Mitigation Strategy. The FDA announcement was based on the interest of the patients who control their diabetes with Avandia. The European Medicine Agency decided to pull Avandia completely off the market, because their country had no system in place to administer a REMS program so it was more cost effective just to remove it from the market. The REMS program, which ensures the access of Avandia is restricted per FDA recommendations, will be available in the near future. On behalf of GlaxoSmithKline, I ask that you table your decision on the TZDs until details of the REMS program are available.

**LISA TRASK:** A representative of Takeda discussed Avandia. On September 23, the FDA announced its decision regarding the continued marketing of Avandia under the highly restricted REMS program. The decision came about following a FDA meeting in July. The committee was convened to discuss the cardiovascular safety of TZDs with the primary focus being Rosiglitazone. Representatives from GSK and the FDA presented specific data on Avandia from several trials, which were reviewed. The outcome concluded that compared to a prescription of Pioglitazone, a prescription of Rosiglitazone was associated with an increased risk of stroke, heart failure, and all cause mortality. Two new meta analyses on Pioglitazone and cardiovascular safety were also presented. The data provided by Takeda included phases two through four studies representing over 22,000 patients. The two studies were different in that the FDA study only included studies that lasted from two months to two years, thus excluding the three-year PROACTIVE study, which was reviewed. Data from these separate and distinct analyses over the past 10 weeks are consistent with and continue to support the Actos label that states there is no increase in mortality or total macro vascular events with Actos.

Dr. Pritchard read a letter from Dr. Andrew Maciejewski regarding the FDA restriction of Avandia. He felt the restricts made it unpractical to retain it on the PDL and recommended preferring Actos in all its dosage forms.

Dr. Pritchard gave the Magellen presentation on TZDs. Avandia and Actos are available in combination with Metformin and Glimepiride. TZDs exert their action by binding and activating the peroxisome proliferator-activated receptor gamma in skeletal muscle, adipose tissue, and the liver, which results in improved insulin action by enhancing the sensitivity of peripheral muscle glucose uptake and possibly reducing hepatic glucose production. Insulin must be present for this to work. TZDs require several weeks to reach maximal benefit. There is a boxed warning regarding causing or exacerbating congestive heart failure in some patients. In December, there were 324 claims: Actos, 90%, and Avandia, 10%. For the combination products, Actos plus Metformin had 17 claims and Avandia plus Metformin had 2 claims. At the last review, a motion declaring the drugs in the class therapeutic alternatives passed seven to three. Significant changes include Actos Plus Met XR is

available. Avandia contains an additional box warning for the possibility of increased risk of myocardial ischemic events such as angina or myocardial infarction. This risk appears to be even higher in patients who are also taking nitrates or insulin.

Dr. Demain noted several physicians recommended shifting from Avandia to Actos on the PDL.

**DR. DEMAIN MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES, TO EXCLUDE ROSIGLITAZONE. SECONDED BY DR. BRIGGS. THE MOTION PASSED UNANIMOUSLY.**

#### **11. Re-review of Renin Inhibitors (Blue Category)**

**FRED AMBURGER:** A representative of Novartis discussed Amturide. The approval of Antrinide was based on data from two studies that showed it provided significantly greater reductions in blood pressure compared to all of the dual combinations of its components. Antrinide is approved for patients whose blood pressure is not adequately controlled with any two of its individual components and is not indicated as initial therapy for high blood pressure. Several studies and their outcomes were reviewed.

Dr. Pritchard gave the Magellen presentation on Renin Inhibitors. Direct renin inhibitors are approved as hypertensives and work by targeting the renin-angiotensin-aldosterone system (RAAS). The most common adverse reaction is diarrhea. These agents have not been studied in patients under 18 years of age. High fat meals decrease absorption and patients should take these drugs at the same time each day. This class is an alternative, but evidence to date does not show a clear advantage over ACEs or ARBs. In December, there were 49 claims: Tekturna, 90%; Valturna, 8%; and Tekturna HCT, 2%. At the last review, a motion for class effect passed unanimously. Significant changes include Tekamlo (ph) was added to the marketplace. It is indicated as initial therapy for hypertension among patients most likely to need multiple drugs to reach blood pressure goal, those not controlled with a single agent, or as a substitute for those on the individual components. It is a pregnancy category D. No dosage adjustments are needed in mild to moderate renal or hepatic impairment, but titration should occur slowly in patients with hepatic impairment. Antrinide, which is a triple combination, was also added to the marketplace.

**MR. GREEAR MOVED A CLASS EFFECT. SECONDED BY DR. DEMAIN. THE MOTION PASSED UNANIMOUSLY.**

#### **12. Re-review of ACE Inhibitors (Green Category)**

Dr. Pritchard gave the Magellen presentation on ACE Inhibitors. These agents can be used as first line therapy in the treatment of hypertension. ACE inhibitors have been shown to slow the progression of diabetic nephropathy, reduce mortality in CHF, and reduce risk of adverse cardiovascular outcomes in high-risk patients. The mechanism of action for ACE inhibitors was described. In December, there were 2,049 claims: Lisinopril, 90%; Enalapril, 4%; Benazepril, 2.6%; Ramipril, 2.29%; Quinapril, 0.6%; and the rest were single digit or zero claims. For the combination products of ACE Inhibitor and Diuretic: Lisinopril HCTZ, 95%; Enalapril HCTZ, 4%; Benazepril HCTZ, 1%; and Quinapril HCTZ, 0.5%. At the last review, a motion for class effect, preferentially including Lisinopril, passed unanimously.

**MS. STABLES MOVED A CLASS EFFECT. SECONDED BY DR. BRIGGS. THE MOTION PASSED UNANIMOUSLY.**

**13. Re-review Alpha Glucosidase Inhibitors (Green Category)**

Dr. Pritchard gave the Magellen presentation on Alpha Glucosidase Inhibitors. The 2009 update to the Consensus Algorithm does not list these drugs, citing relative clinical inferiority with respect to lowering glucose levels. However, these agents are an option for those select patients to assist with glycemic control. These agents are add-on therapy for type II diabetics once other treatments are found to be insufficient or are not tolerated. The mechanisms of the agents were reviewed. In December, there were 8 claims: Precose, 64%, and Acarbose, 37%. At the last review, a motion for class effect passed unanimously.

**DR. BERGESON MOVED A CLASS EFFECT. SECONDED BY MR. GREAR. THE MOTION PASSED UNANIMOUSLY.**

**14. Re-review of Amylin Analogues (Green Category)**

Dr. Pritchard gave the Magellen presentation on Amylin Analogues. Symlin is indicated for patients with type I or type II diabetes who are using insulin, but fail to achieve glycemic control. The mechanism of action of Symlin was reviewed. The most common side effect is mild transient nausea. In December, there was 1 claim for the Symlin pen as the vial is no longer available. At the last review, all of the hypoglycemic, incretin enhancers/mimetics were reviewed together. A motion declaring the drugs in the class as therapeutic alternatives passed unanimously. This year, this is the only drug in class.

**DR. BRIGGS MOVED A CLASS EFFECT. SECONDED BY DR. PHILLIPS. THE MOTION PASSED UNANIMOUSLY.**

**15. Re-review of Androgenic Agents (Green Category)**

Dr. Pritchard gave the Magellen presentation on Androgenic Agents. Testosterone levels are associated with diurnal rhythm; the highest levels occur during the early morning hours. Testosterone supplementation can maintain secondary sex characteristics, optimize bone density, and restore fertility. Oral forms are ineffective due to first pass metabolism. Injectable and transdermal are ideal delivery methods. Some symptoms of low testosterone are impotence, fatigue, mood depression, and regression of secondary sex characteristics depending on the patient's age at time of onset. There appear to be no differences in efficacy as all three agents produce increased levels of circulating testosterone. The gel formulations show a lower incidence of adverse reactions related to administration compared to patches. In December, there were 14 claims: Androgel, 86%; Androderm, 7.14%; and Testim, 7.14%. The significant changes include patients with BPH treated with androgens are at an increased risk for worsening signs and symptoms of the disease. Patients treated with androgenic agents are also at an increased risk for developing prostatic carcinoma. I do not have what the previous discussion was for these agents.

**DR. PHILLIPS MOVED A CLASS EFFECT. SECONDED BY DR. BRIGGS. THE MOTION PASSED UNANIMOUSLY.**

*Break from 9:25 a.m. to 9:41 a.m.*

**16. Re-review of Beta Blockers - Oral (Green Category)**

Dr. Pritchard gave the Magellen presentation on Beta Blockers - Oral. This class has various indications. All have the indication for hypertension with similar efficacy. Other indications vary by drug. Beta-blockers are no longer suggested as first line therapy for the treatment of hypertension. In December, there were 2,068 claims: Atenolol, 28%; Metoprolol Succinate, 21%; Metoprolol Tartrate, 13%; Carvedilol, 11%; and the rest were less than 10%. At the last review, a motion for class effect passed unanimously. The only significant change was initiation of high dose Metoprolol Succinate should be avoided in those undergoing non-cardiac surgery due to impairing the ability of the heart to react to reflex adrenergic stimuli.

In response to Dr. Hope's question regarding the exclusion of Atenolol from the PDL two years ago, Dr. Pritchard said Atenolol was not a preferred agent on the PDL, but still had the most claims. Mr. Greear said Atenolol was not excluded from the PDL, but was restricted and current patients were grandfathered.

**MR. GREEAR MOVED A CLASS EFFECT. SECONDED BY DR. DEMAIN. THE MOTION PASSED UNANIMOUSLY.**

**17. Re-review Benzoyl Peroxide/Clindamycin Combos (Blue Category)**

Dr. Pritchard gave the Magellen presentation on Benzoyl Peroxide/Clindamycin Combos. Benzoyl Peroxide is useful either as a single agent or in combination with antibiotics or retinoids to decrease the number of lesions in mild to moderate acne. In December, there were 81 claims: BenzaClin, 55%; Duac CS, 27%; the generic of BenzaClin, 13.58%; BenzaClin Care Kit had 3 claims. At the last review, a motion for class effect passed unanimously.

**DR. BERGESON MOVED A CLASS EFFECT. SECONDED BY MS. STABLES. THE MOTION PASSED UNANIMOUSLY.**

**18. Re-review of Calcium Channel Blockers (Green Category)**

Dr. Pritchard gave the Magellen presentation on Calcium Channel Blockers. This class is available in combinations with ACE Inhibitors, ARBs, and Atorvastatin. All of these drugs, except for Nimodipine, are indicated for the treatment of hypertension. However, they are not generally used as first line agents. Amlodipine is the only agent that can be crushed without altering its once-daily dosing regimen. Studies have found no significant differences between the agents. In December, there were 924 claims: Amlodipine, 90%; Nifedipine ER, 17 claims; and the rest are less. In the Nondihydropyridine category: Diltiazem CD, 36%; Verapamil, 32%; Diltiazem ER, 16%, and all the rest were single digit or zero claims. For ACE inhibitor calcium channel blocker combinations: Lotrel, 65%; the combination of Amlodipine and Benazepril, 32%; and one or zero claims for the remaining agents. For the ARB calcium channel blocker combinations: Xforge, 84%, and Xforge HCT, 16%. At the last review, a motion declaring the drugs in the class as therapeutic alternatives passed unanimously.

**DR. DEMAIN MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY DR. PHILLIPS. THE MOTION PASSED UNANIMOUSLY.**

**19. Re-review of Biguanides (Green Category)**

Dr. Pritchard gave the Magellen presentation on Biguanides. Initially, type II diabetes does not produce visible symptoms, which can result in delayed diagnosis. Metformin can reduce the HBA1C by 1.5 to 2 percent and can decrease fasting glucose levels up to 20 percent. Metformin also has favorable effects on triglycerides, total cholesterol, and LDL. The 2009 Consensus Algorithm states that along with lifestyle modifications, Metformin should be initiated at the time of diagnosis of type II diabetes. Metformin has a bioavailability of 50 to 60 percent, but this decreases with increasing doses due to a decrease in absorption. The drug is eliminated by the kidney with no hepatic metabolism. In December, there were 1,182 claims: Metformin, 85%; Metformin ER, 15%; and Glucophage, Glucophage XR and Riomet had single digit or no claims. At the last review, a motion to include both immediate release and extended release Metformin tablets passed unanimously.

**DR. KILEY MOVED TO INCLUDE BOTH IMMEDIATE RELEASE AND EXTENDED RELEASE METFORMIN TABLETS ON THE PDL. SECONDED BY MS. STABLES.**

Dr. Briggs spoke against the motion and felt it should be a class effect.

**THE MOTION FAILED WITH NINE OPPOSED.**

**DR. BRIGGS MOVED A CLASS EFFECT. SECONDED BY MR. GREEAR . THE MOTION PASSED UNANIMOUSLY.**

**20. Re-review of Insulins (Green Category)**

Dr. Pritchard gave the Magellen presentation on Insulins. Exogenous insulin supplements deficient levels of insulin when the body cannot produce enough. Insulin is needed to properly utilize carbohydrates, fats, and proteins. Insulin products are used when glycemic control with oral agents is not attained. All insulins can cause a shift in potassium from the extracellular to intracellular space, possibly leading to hypokalemia. Use with caution in patients with risk for this. All insulins need to be dose adjusted in patients with either renal or hepatic impairment. Rapid acting insulins and glargine expire in 28 days. Levemir is good for 42 days. In December, there were 829 claims. For long-acting insulins, there were 427 claims: Lantus vial, 52%; Lantus SolasStar (ph), 40%; and the other were Levemir pen, Levemir vial, and Lantus cartridge. For rapid acting insulins, there were 303 claims: Novolog flex pen, 32%; Novolog vial, 30%; and Humalog vial, 20%. For insulin mixes, there were 24 claims: Novolog 70/30 vial, 30%; and Novolog mix 70/30 flex pen, 25%. For the insulin 70/30: Novolog vial, 79%; and Humulin vial, 16%. Insulin N: Novolin N vial, 62%; and Humulin N vial, 40%. Insulin R: Humulin R vial, 52%; and Novolin R vial, 48%. Humulin U-500 is now available, but is not commonly used in a retail setting due to its concentration. At the last review, a motion for class effect, preferentially including Lantus, passed unanimously.

Dr. Demain said that a sliding scales were setup for Regional Alaska, Providence Hospital and Alaska Native Medical Center last year using Lantus as their protocol, so it is probably important to retain

Lantus on the PDL. Dr. Briggs felt the committee was supposed to evaluate the therapeutic value of the drugs, not what was being used. Mr. Greear noted that although Levemir claims to be a once a day formulation, it is generally administered twice a day. Lantus is truly a once daily formulation, which is why it was preferred. Dr. Demain pointed out that the committee has won the respect of their colleagues by taking into consideration legitimate requests and desires, and should continue to do so.

**DR. DEMAIN MOVED A CLASS EFFECT, PREFERENTIALLY INCLUDING LANTUS. SECONDED BY DR. PHILLIPS. THE MOTION PASSED WITH TWO OPPOSED.**

## **21. Re-review of Glaucoma Agents (Green Category)**

Dr. Pritchard gave the Magellen presentation on Glaucoma Agents. Glaucoma is the second most common cause of blindness in the U.S. and the most common cause among African-Americans. Caucasians have a steeper rise in open-angle glaucoma associated with age, which occurs more frequently in men. Increased ocular pressure alone is not considered diagnostic for glaucoma. There are two types of glaucoma: open-angle and closed-angle. Medications used include beta-blockers, miotics, sympathomimetics, topical carbonic anhydrase inhibitors, and prostaglandin analogs. Monotherapy or combination therapy can be used to treat glaucoma. No guidelines suggest any one class should be first line agents, but prostaglandin analogs may be the most effective drugs, reaching up to 30 percent reduction of intraocular pressure. In December, there were 78 claims, which were broken down into subclasses. For the alpha 2 androgenic agents, Alphagan P had 7 claims. For beta-blockers, Timolol had 33%, Combigan had 27%, and the rest were 10 percent or less. For carbonic anhydrase inhibitors, Dorzolamide/Timolol combination had 4 claims. For prostaglandin analogs, Xalatan had 50%, Travatan Z had 44%, and Lumigan had 0.03%. At the last review, a motion declaring the drugs in the class as therapeutic alternatives passed unanimously.

**DR. BERGESON MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY DR. BRIGGS. THE MOTION PASSED UNANIMOUSLY.**

## **22. Re-review Metglinides (Green Category)**

Dr. Pritchard gave the Magellen presentation on Metglinides. These agents are used for type II diabetes. They help lower glucose levels by stimulating insulin release from the pancreas by binding to non-sulfonylurea binding sites on the beta cells, which closes the ATP dependent potassium channels, leading to calcium channel opening. The increased calcium induces insulin secretion. This process is highly selective with little effect on heart or skeletal muscle tissue. Both agents are contraindicated in type I diabetes. Prandin is also contraindicated in patients taking Gemfibrozil. In December, there were 2 claims: Nateglinide 50%, and Starlix, 50%. At the last review, a motion for class effect passed unanimously.

**DR. BERGSON MOVED A CLASS EFFECT. SECONDED BY DR. KILEY. THE MOTION PASSED UNANIMOUSLY.**

**23. Re-review of Topical Anesthetics (Green Category)**

Dr. Pritchard gave the Magellen presentation on Topical Anesthetics. The Lidoderm patch is indicated for use in patients with post herpetic neuralgia. Lidoderm has varied absorption depending on the duration of application and surface area. Only 3 percent of the applied dose is expected to be systemically absorbed. Lidocaine is approximately 70 percent protein bound and is metabolized rapidly through the liver to several metabolites, which are then renally excreted. Use of Lidoderm with a heat source should be avoided. Up to three patches may be applied to the affected area for up to 12 hours in a 24-hour period. Since about 95 percent of the drug is left in the patch, disposal out of the way of children and pets is recommended. In December, there were 189 claims. At the last review, a motion for class effect passed unanimously.

**DR. DEMAIN MOVED A CLASS EFFECT. SECONDED BY DR. BERGESON. THE MOTION PASSED UNANIMOUSLY.**

**24. Re-review of Topical Immunomodulators (Green Category)**

Dr. Pritchard gave the Magellen presentation on Topical Immunomodulators. Atopic dermatitis is a chronic inflammatory disease of the skin. It is from a combination of genetic and environmental factors. It is also referred to as eczema. Most patients have a mild form involving less than 20 percent of their skin. Atopic dermatitis can develop at any age, but the majority of cases develop before age 5. These agents exert action on the T-cells by suppressing cytokine transcription, which leads to a decrease in skin inflammation. A significantly greater number of patients were successfully treated with Protopic than those treated Elidel. Both had the same incidence of burning and itching at application site. Rare cases of malignancies have been reported with both agents so the FDA recommends short-term, intermittent use. No one product demonstrates a clear advantage over the other. In December, there were 100 claims: Elidel had 57 claims and Protopic had 43 claims. At the last review, a motion declaring the drugs in the class as therapeutic alternatives passed unanimously.

**DR. BERGESON MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY DR. DEMAIN.**

Dr. Demain said Elidel was typically used for younger children as a first step. Elidel seems to be better tolerated when a child's dermatitis is angrier. Protopic is more potent and often used as a second step therapy. A lot more burning is reported with Protopic as compared to Elidel. The pattern of usage has change over the last nine months and the current recommendation is to use it twice a day for two weeks until you go into remission and then use it twice a week to maintain the remission. When the condition reoccurs, repeat the process.

**THE MOTION PASSED UNANIMOUSLY.**

**25. Re-review of Topical Retinoids (Green Category)**

Dr. Pritchard gave the Magellen presentation on Topical Retinoids. Since 2009, guidelines have recommended that topical retinoids be the foundation of treatment for acne as they target the microcomedone, the precursor to all acne lesions. When used from the beginning of therapy, retinoids significantly increase the speed of resolution of acne lesions. Retinoid monotherapy or in combination

with benzoyl peroxide is recommended as maintenance therapy. In December, there were 65 claims: Epiduo, 22%; Tretinoin, 20%; and all the rest were single digit or zero claims. At the last review, a motion for class effect passed unanimously.

**DR. KILEY MOVED A CLASS EFFECT. SECONDED BY DR. DEMAIN. THE MOTION PASSED UNANIMOUSLY.**

## **26. Re-review of Sulfonylureas**

Dr. Pritchard gave the Magellen presentation on Sulfonylureas. These agents enhance response of beta cells in the pancreatic islet to glucose. They bind to the plasma membrane of functioning beta cells, resulting in a decrease in potassium permeability that increases membrane depolarization and therefore causes an influx of calcium ions. This results in secretion of insulin and subsequent lowering of blood glucose. This class is efficacious, well tolerated, and dosed once daily. In addition to insulin and TZDs, these drugs are treatment options after failure of Metformin to adequately treat hyperglycemia. Non-micronased and micronased Glyburide cannot be used interchangeably. Glipizide ER is not for use in patients with GI motility problems such as strictures, obstructions, or severe narrowing. In December, there were 491 claims: Glyburide, 37%; Glipizide, 25%; Glimepiride, 19%; and all the rest were less than 10 percent. At the last review, a motion declaring the drugs in the class as therapeutic alternatives passed with one abstention.

**DR. KILEY MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY DR. BERGESON.**

Ms. Stables questioned why the drugs were declared therapeutic alternatives. There are times when Glipizide is used over Glyburide, such as with renal dysfunction in elderly patients. There are times when the XL formulation is better than the IR formulation. Some patients feel Glimepiride does a better job of controlling blood glucose. All of the mechanisms of action are similar and the outcomes are the same. The committee discussed whether using the term therapeutic alternatives rather than class effect would make a difference in the bid process. Mr. Campana said most of the drugs were generics so there would be no major cost differential.

**THE MOTION PASSED WITH ONE OPPOSED.**

## **27. Re-review of Ulcerative Colitis - Oral**

Dr. Pritchard gave the Magellen review of Ulcerative Colitis - Oral. The recommendations for maintenance and remission in distal disease include mesalamine suppositories in patients with proctitis and mesalamine enemas in patients with distal colitis, when dosed as infrequently as every third night. Sulfasalazine, mesalamine compounds, and balsalazide are also effective in maintaining remission. The combination of oral and topical mesalamine is more effective than either one alone. Patients with active disease should begin therapy with oral Sulfasalazine or an alternative aminosalicilate. Asacol HD 800 milligrams is not equivalent to two of the 400 milligrams so do not substitute. In December, there were 87 claims: Asacol, 40%; Sulfasalazine IR, 37%; Pentasa, 16%; and all the rest were 2 percent or less. At the last review, a motion declaring the drugs in the class as therapeutic alternatives, to include one Sulfasalazine and one delayed release product, passed unanimously.

**DR. KILEY MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES, TO INCLUDE ONE SULFASALAZINE AND ONE DELAYED RELEASE PRODUCT. SECONDED BY DR. BERGESON. THE MOTION PASSED UNANIMOUSLY.**

**28. Review Minutes from November 2010 Meeting**

Mr. Campana reviewed the corrections to November 2010 meeting minutes.

**DR. BERGESON MOVED TO APPROVE THE NOVEMBER 2010 MEETING MINUTES AS CORRECTED. SECONDED BY DR. BRIGGS. THE MOTION PASSED UNANIMOUSLY.**

**29. Comments from Committee Members or Chair**

Mr. Campana said the preferred drug list and the P&T Committee was coming to a crossroads. Due to the healthcare reform, the rebate structure would be changing and it may not be advantageous to maintain some of the classes on the PDL. Based on the new rebates, it might be better for the state to use a different editing system for PPIs, statins, and other classes. As we go forward, classes may be removed from the PDL, as well as others added when the opportunity arises. The changed rebate structure under the healthcare reform was explained.

Dr. Demain discussed the Supreme Court's decision that state retained the right to opt out of the healthcare reform. The committee discussed how rebates would be affected if Alaska opted out.

Mr. Campana said Alaska could opt out of the benefits, but not the cost. CMS is already calculating the offset amount. From what we have seen over the past years, our rebates have gone up and we know that CMS will be taking a greater share of those rebates. The environment is changing, but we will move forward and work with it as best we can.

Dr. Malter said that even though some of the classes might be removed from the PDL, the state would still keep control over the costs through other approaches such as the DUR.

Mr. Campana said there were ways to promote an advantage to the state and still end up with lower medication costs for the Medicaid community and overall savings for the program. The drug classes to be reviewed at the next meeting were listed.

Dr. Brodsky noted that he would not be available for the next meeting.

**28. Adjourn**

**MR. GREAR MOVED TO ADJOURN THE MEETING. SECONDED BY DR. DEMAIN. THE MOTION PASSED UNANIMOUSLY.**

The meeting adjourned at 10:31 a.m.