ALASKA MEDICAID
PHARMACY AND THERAPEUTICS COMMITTEE

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

MINUTES OF MEETING
January 17, 2014
8:00 a.m.

Committee Members Present:
Robert Carlson, MD (telephonic)
Robin Cooke, Pharm.D.
Jeffrey Demain, MD
Vincent Greear, R.Ph.
Diane Liljegren, MD (telephonic)
Jenny Love, MD
John Pappenheim, MD (telephonic)
Claudia Phillips, MD
Maggi Rader, CNM
John Riley, PA-C
Greg Salard, MD (telephonic)
Chuck Semling, Pharm.D.
Trish White, R.Ph. (telephonic)

Committee Members Absent:
Marvin Bergeson, MD
Jill Reid, R.Ph.

Others Present:
Erin Narus, Pharm.D., Magellan Medicaid Administration
Chad Hope, Pharm.D.

1. Call to Order – Chair

Dr. Demain called the meeting to order at 8:06 a.m.

2. Roll Call

A quorum was present. Dr. Demain welcomed everyone to the first meeting in 2014 and reviewed how the meeting would proceed. Dharma Begich has rotated off the committee. Robin Cooke, Pharm.D., from Providence Hospital has joined the committee.

3. Public Comments - Local Public/Health Practitioners

DR. NOLAN: Had a family practice in Anchorage from 1977 to 1979, left for five years for additional training, returned to Anchorage, and has been an endocrinologist since 1983. He has no financial involvement in the issues being discussed and attended the meeting voluntarily. Dr. Nolan asked that Liraglutide be included on the PDL as it is very effective for patients with type 2 diabetes. Several recent studies and their outcomes were discussed. In November 2012, there was a randomized open-label study comparing long-acting Exenatide and Liraglutide. Liraglutide was found to be more effective for glycosylated hemoglobin levels. In 2010, a study published in Diabetes Care reported that Liraglutide had increased beneficial glycemic control as compared to Exenatide. Liraglutide should be included on the PDL as it is dispensed once a day, is extremely effective and does not have to be adjusted for renal sufficiency. For insulin delivery systems, the uses of pens, rather than vials, are encouraged due to the pen's accuracy, convenience and patient preferences. A new Medtronic MiniMed insulin pump called the Enlite was discussed. The pump has a suspense system with a closed-loop system for insulin delivery. It is very effective, particularly for patients with neuroglycopenia hypoglycemia with counter regulatory abnormalities, which are common for long-standing type 1 diabetic patients, as well as some type 2 patients or so-called type 1.5 patients. It is very beneficial for pregnant patients, because the suspense system stops delivery of insulin when the glucose reaches whatever level has been programmed into the pump.

Dr. Hope said the insulin pumps were addressed in the Durable Medical Equipment Program, which was recently moved back into his department.

In response to Dr. Demain, Dr. Nolan felt the committee was effective and did good work.

4. Re-review of Anticoagulants (Red Category)

DAVID GROSS: A representative of Pfizer discussed Eliquis (Apixaban). Eliquis is a factor Xa inhibitor that is indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation. Several trials and their outcomes on the efficacy and safety of Eliquis were reviewed. The boxed warning states that Eliquis should not be discontinued abruptly without switching to another anticoagulant due to potential strokes. Eliquis should not be used in patients with active pathologic bleeding or a hypersensitivity to the product. Eliquis was not studied in patients with prosthetic heart valves. The most common adverse reactions were reviewed. If a surgical procedure is evasive with a moderate to high risk of unacceptable or clinically significant bleeding, Eliquis should be discontinued 48 hours before surgery; for surgeries with less bleeding, it should be discontinued 24 hours prior to surgery.

In response to Dr. Demain, Mr. Gross said there were ongoing studies for the use of Eliquis in orthopedic cases. More information on those studies will be available at the next review.

STEVE HALL: A representative of Boehringer Ingelheim discussed Dabigatran (Pradaxa), which has been on the market since its approval by the FDA in the fall of 2010. It has been prescribed by more than 20,000 cardiologists for U.S. patients with more than 5.5 million prescriptions filled. Dabigatran is indicated to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation. The overall risk of stroke is five times greater in patients for atrial fibrillation. For all patients, nine out of 10 strokes are ischemic strokes. Several studies and their outcomes were reviewed. The risk of stroke and bleeding increases with age, but the risk versus benefit profile is favorable in all age groups. The FDA conducts ongoing surveillance and monitoring of the safety and efficacy of

Dabigatran, which was described. Dabigatran is superior in reducing strokes relative to Warfarin, and it has similar rates of major bleeding. It is the first and only anticoagulant to show superiority in reducing both ischemic and hemorrhagic strokes relative to Warfarin in patients with nonvalvular atrial fibrillation.

BOB JENIKER: A representative of Janssen discussed Rivaroxaban (Xarelto), which clearly has a broad base of indications including orthopedic surgery, the prevention of the occurrence of DVT, the reduction and risk of stroke in patients with nonvalvular atrial fibrillation, as well as the treatment of DVT PE and the prevention of recurrence thereof. Several studies and their outcomes were reviewed. DVT patients given Xarelto often have a shorter duration of hospitalization. In addition, PE patients given Xarelto have shorter durations of hospitalization of one day. The FDA recently reviewed data for Xarelto in the treatment of patients with acute coronary syndrome, and we anticipate a new indication in the future.

In response to Dr. Demain, Dr. Hope said it was difficult to calculate the cost savings associated with not monitoring INR. Mr. Jeniker said cost savings in the reduction in INR was not mitigated by an increased expense of Xarelto. As new data is presented, we expect to see a high degree of persistency associated with coagulants versus Warfarin, which could also prevent events.

In response to Dr. Demain, Mr. Jeniker and Mr. Hall discussed reversal agents that were currently in development. Mr. Hall said he would be happy to submit additional information to the committee on this topic.

Ms. Narus gave the Magellan presentation on Anticoagulants. The agents in this class are indicated for the prevention of DVT and DVT treatment with or without PE. There are three newer oral agents, as well as Warfarin and a few injectable agents within this class. The 2012 American Heart Association and American Stroke Association said Warfarin, Dabigatran, Rivaroxaban and Apixaban were all indicated for the prevention of first and recurrent strokes in patients with nonvalvular atrial fibrillation, and that the selection of these drugs should be individualized on the basis of risk factors, cost, tolerability, patient preference, potential for drug interactions and other clinical characteristics. They suggest that renal dosing be taken into consideration for Dabigatran and Rivaroxaban, which are considered efficacious alternatives to Warfarin. In October 2013, there were 276 claims: 70.7% for Warfarin, 8.3% for Coumadin, 7% for the injectable Enoxaparin, and down from there. Utilization for the new oral agents were: 5.8% for Xarelto, 3.3% for Pradaxa and no utilization for Eliquis. In December 2013, an analysis was posted discussing the favorable risk benefit for the newer oral agents for atrial fibrillation with respect to their safety profiles. At the last review, a motion for therapeutic alternatives to include at least one oral agent, one injectable agent and Warfarin passed unanimously.

Dr. Hope noted that while most of the conversation was about the newer agents, the current review is for both the oral and injectable agents.

DR. LILJEGREN MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES, TO INCLUDE ONE ORAL AGENT AND ONE INJECTABLE AGENT, AND TO INCLUDE WARFARIN.

The committee discussed the motion. Dr. Hope said that most of the rural areas of Alaska where monitoring of INR was not available, patients were covered by the Tribal Health System so usage

depended on which drugs were on their formularies. Mr. Riley noted that the non-preferred agents could be prescribed utilizing the medically necessary clause. Dr. Liljegren felt it was important to include an agent on the PDL that did not require monitoring. Dr. Hope said the DUR Committee reviewed the newer oral agents and has a prior authorization requirement to restrict the use to the labeled indications. Lovenox and Fragmin do not have hard PAs. Dr. Phillips said the Alaska Native populations that required these types of drugs probably had additional funding other than Indian Health Service funding. She felt there should be a drug on the PDL that did not require INR.

SECONDED BY DR. SEMLING. THE MOTION PASSED WITH TWO OPPOSED.

5. Re-Review of Lipotropics (Other): Omega-3 Fatty Acids (Red Category)

There were no public testimonies.

Ms. Narus gave the Magellan presentation on Lipotropics, Other: Omega-3 Fatty Acids. Both agents in this group are FDA approved for the treatment of hypertriglyceridemia in adults with severely elevated triglycerides such as those greater than 500 milligrams per deciliter. Lovaza is in combination of 465 milligrams of EPA and 375 milligrams of DHA. The medium increase in LDL with this agent is approximately 49 percent over placebo. Decreases in triglycerides were up to 45 percent if the triglycerides were greater than 500 during studies. LDL monitoring is advised with this agent. Vascepa contains 4 grams of icosapent ethyl. It does not contain a DHA component. There was no appreciable increase in LDL over placebo in the studies. Median decrease in triglycerides was up to 33 percent over placebo. The effects of Icosapent Ethyl and Omega-3-Acid Ethyl Esters on cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia have not been determined. The risk effect of these agents for pancreatitis in patients with severe hypertriglyceridemia has not been explicitly determined. There is no REMS monitoring required for these agents. Safety and efficacy has not been established in patients. They are both pregnancy category Cs. Both of the agents are given with food and should be swallowed whole. In October 2013, there were 26 claims for Lovaza. Several trials and their outcomes were reviewed. This is the first review where these drugs were broken into subgroups. At the last review of all of the other Lipotropics, a motion for therapeutic alternative to include at least one triglyceride lowering agent and one bile acid sequestrants passed.

DR. PHILLIPS MOVED A CLASS EFFECT. SECONDED BY DR. LOVE.

The committee discussed the motion. Dr. Liljegren expressed concern that Lovaza was over used due to its LDL effect, and felt Vascepa was a superior drug even though it did not lower LDL as much. She did not feel the drugs were equivalent. Dr. Hope did not know if there was any long-term outcome data related to cardiovascular mortality. Ms. Narus said the ACCHA Guidelines stated these agents were not considered initial monotherapy, but adjunctive types of therapies. Dr. Demain said there has been a lot of emphasis recently on DHA, which along with the Omega-3s appears to be more effective in cardiovascular protection. Dr. Liljegren did not feel any of the drugs in this class should be preferred.

WITHOUT OBJECTION, THE MOTION PASSED UNANIMOUSLY.

6. Re-Review of Lipotropics (Other): Apo Lipoprotein B Synthesis Inhibitors (Red Category)

There were no public testimonies.

Ms. Narus gave the Magellan presentation on Lipotropics (Other): Apo Lipoprotein B Synthesis Inhibitors. Both agents in this group are FDA approved for the reduction of LDL-C, total cholesterol, Apo-B, and non-HDL-c in patients with homozygous familial hypercholesterolemia as an adjunct to diet and lipid-lowering medications and treatments. Familial hypercholesterolemia is a genetic disorder that leads to accumulation of LDL particles in plasma and premature cardiovascular disease. It is generally a rare situation, occurring in one out of a million people in the United States. In these situations, the LDL receptor activity is nearly absent and LDL-C levels commonly range between 400 and 1,000 milligrams per deciliter. Apo-B is a structural protein of VLDL and LDL. Lomitapide (Juxtapid) directly binds and inhibits MTP, thus preventing the synthesis of apo-B in enterocytes and hepatocytes. This results in decreased synthesis of VLDL, and thereby reduces plasma LDL-C levels. Mipomersen (Kynamro) is an antisense oligonucleotide, complementary to the coding region of the human messenger ribonucleic acid for apo-B-100, which is the principal apo lipoprotein of LDL. Mipomersen binds to the mRNA forming hybridization to the mRNA that results in the degradation of that complex and inhibiting the translation of the apo B-100 protein. Both agents are contraindicated in moderate to severe hepatic impairment. There is a black boxed warning due to risk of hepatotoxicity resulting in transaminases and hepatic steatosis. Baseline labs are needed monthly for the first year. Alcohol should be avoided or at least limited to no more than one drink per day. It is also advised to avoid other hepatotoxicity drugs. Juxtapid is contraindicated in pregnancy. There are risks of nutritional deficiencies with Juxtapid. Daily supplementation of vitamin E, linolenic acid, alpha-linolenic acid, EPA and DHA are recommended. Both agents are only available through a restricted access program, which exists to inform prescriber about the hepatotoxicity risks and to restrict access to those with clinical or lab diagnosis consistent with the homozygous familial hypercholesterolemia and may only be prescribed and dispensed by certified prescribers and pharmacies. A REMS prescription authorization form is required for each new prescription. Juxtapid is an oral agent that is swallowed whole without food two hours after the evening meal, whereas Kynamro is administered subcutaneously once weekly. For Juxtapid, CYP3A4 inhibitors increase its exposure. Warfarin exposure is also increased via this agent. Kynamro has no CYP450 interactions and does not interact with Warfarin. As noted above, Juxtapid has a pregnancy category X. Kynamro has a pregnancy category of B. Safety and efficacy has not been established in pediatrics. In October 2013, there was no utilization of these products in 2013. These are new agents and a new subgroup so there was no prior review.

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

6. Re-Review of Hypoglycemics, Incretin Enhancers/Mimetics (Red Class)

STEVE HALL: A representative of Boehringer Ingelheim discussed Tradjenta, a DPP-4 inhibitor. It is indicated as an adjunct to diet and exercise to improve glycemic control in type 2 diabetes melodious. It should not be used in patients with type 1 diabetes or for the treatment of diabetic hetoacidosis. Tradjenta is approved at one dose for patients with type 2 diabetes at 5 milligrams once daily. It can be taken with or without food. No dosage adjustment is recommended for patients with renal or hepatic impairment. It has been studied as monotherapy in combination with Metformin, sulfonylureas, Pioglitazone, insulin, and in patients with renal impairment. Several studies and their outcomes were reviewed. Reported adverse reactions were reviewed.

Ms. Narus gave the Magellan presentation on Hypoglycemics, Incretin Enhancers/Mimetics. The DPP-4 enzyme inactivates GLP-1 and GAP, thus inhibiting the DPP-4 enzyme. These agents slow the inactivation of incretins and prolong their action. DPP-4 inhibitors are FDA indicated as adjuncts to diet and exercise to improve glycemic control in adults with type 2 diabetes. Combination products should only be used when treatment with both agents are appropriate. In 2011, the REMS for Januvia and Janumet were removed. Renal function has been monitored with some of these agents, specifically Sitagliptin. Contraindications for the newer agents came out in 2013, which were reviewed. Juvisync is a pregnancy category X. Oseni is a pregnancy category C. The other agents are pregnancy category B. No data is available in pediatric populations at this time. In October 2013, there were 150 claims: 69% for Januvia and 18% for Janumet. Significant changes include a release from the American Academy of Clinical Endocrinologists of a new algorithm and consensus statement for the treatment of type 2 diabetes. Juvisync was voluntarily discontinued due to business reasons and not safety concerns. All products currently in distribution will reach expiration by October 2014. As noted in a previous discussion regarding acute pancreatitis, the American Diabetes Association and the American Association of Clinical Endocrinologists suggested that new findings for this reaction should not change the treatment of patients with diabetes. Any concerns should be addressed on a patient-by-patient level. In January 2013, this was a broader class and not broken out into subgroups. At the last review, a motion to split out the GLPs and the DPP-4s into separate categories passed, and then separate motions for class effect passed unanimously.

DR. LILJEGREN MOVED A CLASS EFFECT. SECONDED BY MR. RILEY. THE MOTION PASSED UNANIMOUSLY.

Break from 9:07 a.m. to 9:16 a.m.

7. Re-Review Angiotensin Modulators: ACE Inhibitors and Renin Inhibitors (Green Class)

Ms. Narus gave the Magellan presentation on Angiotensin Modulators: ACE Inhibitors and Renin Inhibitors. ACE inhibitors and direct renin inhibitors are combined in this subgroup. ACE inhibitors 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 the risk of adverse cardiovascular outcomes in high-risk patients. Direct renin inhibitors are approved as an antihypertensive and work by targeting the renin angiotensin aldosterone system at the point of activation, thereby lowering blood pressure through decreasing plasma renin activity. This class is an alternative, but evidence to date does not show clear advantages over ACE inhibitors or ARBs. In October 2013, there were 2,151 claims with 84.3% for Lisinopril. Significant changes were reviewed. Epaned is new to the marketplace. Aliskiren (Tekturna) and Aliskiren-containing products are contraindicated with ARBs or ACE inhibitors, as well as in patients with diabetes due to increase of renal impairment, hypokalemia and hypotension. It is advised to avoid the use of Aliskiren with ARBs, especially in patients with renal impairment. At the last review, a motion for therapeutic alternatives to include at least one drug from each subgroup passed unanimously.

MS. RADER MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES TO INCLUDE AT LEAST ONE DRUG FROM EACH SUBGROUP. SECONDED BY MR. RILEY. THE MOTION PASSED UNANIMOUSLY.

8. Re-review of Angiotensin Modulators: Angiotensin Receptor Blockers (Green Class)

Ms. Narus gave the Magellan presentation on Angiotensin Modulators: Angiotensin Receptor Blockers. Angiotensin II receptor blockers share an indication for hypertension. Some hold additional indications for nephropathy or heart failure. ARBs block the vasoconstrictor and aldosterone secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT-1 receptors. In October 2013, there were 613 claims: 48.9% for Losartan and 22.5% for Diovan. At the last review, a motion for class effect passed unanimously.

MR. RILEY MOVED A CLASS EFFECT. SECONDED BY DR. PHILLIPS. THE MOTION PASSED UNANIMOUSLY.

9. Re-Review of Lipotropics (Other): Cholesterol Absorption Inhibitors (Green Class)

Ms. Narus gave the Magellan presentation on Lipotropics (Other): Cholesterol Absorption Inhibitors. Ezetimibe (Zetia) inhibits cholesterol absorption along the brush border of the small intestine by targeting the NPC1L1 sterol transporter. It is FDA indicated for primary hypercholesterolemia as monotherapy or in combination with statins. It is also indicated for mixed hyperlipidemia in combination with Fenofibrate and as an adjunct to statin for homozygous familial hypercholesterolemia. Zetia is contraindicated with a statin in acute liver disease. There is a potential risk of cholelithiasis when given in combination with fibric acids. The agent is a pregnancy category C. It may be taken with or without food. In October 2013, there were 113 claims for this agent. This agent was previously grouped under the broader Lipotropics (Other) category and a motion for therapeutic alternatives to include at least one triglyceride lowering agent and one vile acid sequestrant passed.

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

10. Re-Review of Lipotropics (Other): Niacins (Green Class)

Ms. Narus gave the Magellan presentation on Lipotropics (Other): Niacins. Niacin inhibits lipolysis and the hepatic triglyceride production resulting in reduced synthesis. It also increases HDL-C by 15 to 35 percent. Niacin is contraindicated in chronic liver disease, active peptic ulcer disease, and arterial bleeding. There is an increased risk of myopathy when given in combination with statins. INR should be monitored when given in combination with Warfarin. There is no REMS for this agent. It is a pregnancy category C when used for hyperlipidemia treatment. It is to be taken at bedtime after a low-fat snack. Aspirin may be administered prior to the dose to reduce flushing. For the extended release product, the dose may be titrated up every four weeks. In October 2013, there were 50 claims for Niaspan. No utilization is available for the other products. As this is a new subgroup, there was no previous motion.

MR. RILEY MOVED A CLASS EFFECT. SECONDED BY DR. RADER. THE MOTION PASSED UNANIMOUSLY.

The committee discussed potential cardiac ischemic issues with the use of Niacin. Dr. Hope said the study was stopped, because patients were having more cardiac ischemic events.

11. Re-Review of Lipotropics (Other): Fibric Acids (Green Class)

Ms. Narus gave the Magellan presentation on Lipotropics (Other): Fibric Acids. The effects of fibric acids are related to the activation of the PPAR receptor, which increases lipolysis and elimination of TG-rich particles. Fenofibrate and Gemfibrozil can lead to cholelithiasis. Fenofibrates and fibric acids are contraindicated in patients with hepatic or severe renal dysfunction. Gemfibrozil, used with Simvastatin, is not advised and is contraindicated. Fenofibrate does not interfere with statin metabolism and may be less likely to increase the risk for myopathy with moderate doses of statins. Concurrent use with oral hypoglycemics may result in enhanced hypoglycemic effect. These agents are pregnancy category C. Gemfibrozil should be administered 30 minutes prior to a meal. There are various other administration considerations for the other agents in this class with respect to food. In October 2013, there were 228 claims: 30.7% for Gemfibrozil, 31% for Tricor, and down from there. As this is a new subgroup, there was no previous motion.

The committee discussed myopathy, which is associated with the concurrent use of Gemfibrozil and statins, although it can occur without statins as well. Mr. Greear pointed out that Tricor was currently preferred, but not the generics. Dr. Hope said that in rare instances brand-name products were less expensive than the generic versions due to the rebate structure. When this occurs, sometimes the pharmacies do not carry the preferred products. Pricing and supplemental rebates of the drugs was discussed.

DR. LOVE MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY DR. SEMLING. THE MOTION PASSED UNANIMOUSLY.

12. Re-Review of PAH Agents: Pulmonary Arterial Hypertension (PAH) Agents: PDE-5 Inhibitors (Green Class)

Ms. Narus gave the Magellan presentation on Pulmonary Arterial Hypertension (PAH) Agents: PDE-5 Inhibitors. Within this subgroup is Sildenafil (Revatio) and Tadalafil (Adcirca). These agents inhibit PD-5 in the smooth muscle of pulmonary vasculature where PD-5 is responsible for the degradation of cGMP. Increased cGMP concentrations result in pulmonary vasculature relaxation; vasodilatation in the pulmonary bed and systemic circulation can occur. Concurrent administration of organic nitrates (nitroglycerin) in any form with Sildenafil (Revatio) or Tadalafil (Adcirca) is contraindicated as the combination potentiates the hypertensive effects. Sildenafil is not recommended in pediatric patients with PAH, based on a long-term clinical pediatric trial that showed low doses of Sildenafil were not effective in improving exercise ability and a high dose of Sildenafil was associated with higher risks of death. Though treatment of PAH with Sildenafil in children is not an FDA approved indication, the recommendation against its use in this patient population has been added to the study results. Sildenafil may cause serious vaso-occlusive crises. The effectiveness of Sildenafil in pulmonary hypertension secondary to sickle cell anemia has not been established. These agents are pregnancy category B. Both are oral agents. In October 2013, there were 10 claims: 52.9% for Adcirca and 5.9% for Revatio. At the last review, when this was part of the larger group, a motion for therapeutic alternatives to include at least one oral agent and one inhaled agent passed.

In response to Mr. Greear, Dr. Hope said the PD-5 required a prior authorization. The generic for Revatio is much less expensive.

MR. GREEAR MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY DR. RADER. THE MOTION PASSED UNANIMOUSLY.

13. Re-Review of Pulmonary Arterial Hypertension (PAH) Agents: Oral Endothelial Receptor Antagonists (Green Class)

Ms. Narus gave the Magellan presentation on Pulmonary Arterial Hypertension (PAH) Agents: Oral Endothelial Receptor Antagonists. This group includes Ambrisentan (Letairis). Endothelin-1 is a neurohormone whose effects are mediated by binding to receptors in the endothelium and vascular smooth muscle. Increased ET-1 concentrations in the plasma and lung tissue occur in patients with PAH. Two receptor subtypes, ET_A and ET_B, mediate the effects of ET-1 in the vascular smooth muscle and endothelium. Bosentan (Tracleer) is a competitive antagonist to the endothelium receptor A and B subtypes. Ambrisentan (Letairis) is selective to the ET_A receptor. The clinical impact for high selectivity for the ET_A receptor or for the converse, which is the dual blockage, is unknown. Ambrisentan is contraindicated in patients with idiopathic pulmonary fibrosis including IPF patients with pulmonary hypertension. Ambrisentan and Bosentan have a REMS program which includes a Medication Guide, elements to ensure safe use, and implementation systems. Safety and efficacy has not been established in pediatrics. In October 2013, there were two claims for Letairis and one for Tracleer. As this is a new subgroup, there was no previous motion.

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

14. Re-Review of Platelet Aggregation Inhibitors (Green Class)

Ms. Narus gave the Magellan presentation on Platelet Aggregation Inhibitors. These agents are used for a variety of indications, prevention of strokes and TIAs, cardiac event treatment and risk reduction, peripheral artery disease, and to reduce the rate of stent thrombosis. The mechanism of action varies among these products. Clopidogrel requires activation via the CYP2C19 pathway. Patients who have insufficient CYP2C19 activity and those who are taking CYP2C19 inhibitors or substrates may experience a decrease in Clopidogrel efficacy. As of October 2013, the REMS requirement for Ticagrelor (Brilinta) has been removed. Safety and efficacy has not been established in pediatrics for most of these agents. Dipyridamole safety, specifically in ages less than 12, has not been established. Aggrenox is pregnancy category D. Brilinta is pregnancy category C. All the other agents are pregnancy category B. The significant changes were reviewed. Prasugrel and Ticagrelor were added to the ACC/AHA 2013 STEMI Guidelines. Use of Prasugrel is not recommended in STEMI patients with a prior history of stroke and transient ischemic attacks for whom primary PCI is planned. After the placement of a drug-eluting or bare-metal stent, the 2013 ACC/AHA STEMI Guidelines recommend dual antiplatelet therapy with aspirin indefinitely and a $P2Y_{12}$ platelet inhibitor (Clopidogrel, Prasugrel or Ticagrelor) for at least 12 months (Level of Evidence B). It is reasonable to consider continuation of therapy for more than 12 months for patients undergoing drug-eluting stent placement (Level of Evidence C). In STEMI patients with a prior history of stroke and TIA for whom primary PCI is planned, Prasugrel is not recommended as part of the dual-antiplatelet therapy regimen (Level of Evidence C). For utilization, all of the agents are listed together. The listing identifies the agents that have utilization only. Utilization: 86% for Clopidogrel, 5.8% for Plavix, 3.8% for Effient and 4.4% for Aggrenox. At the last review, a motion for therapeutic alternatives to include at least one Clopidogrel or Prasugrel being preferentially included and excluding Ticagrelor.

DR. PAPPENHEIM MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES WITH AT LEAST ONE COPIDOGREL OR PRASUGREL BEING PREFERENTIALLY INCLUDED, AND EXCLUDING TICAGRELOR. SECONDED BY DR. PHILLIPS. THE MOTION PASSED UNANIMOUSLY.

15. Re-Review of Growth Hormone (Green Class)

Ms. Narus gave the Magellan presentation on Growth Hormone. Human growth hormone is a 191-amino acid polypeptide hormone secreted by the anterior pituitary gland. It is administered via IM or SC injection. Treatment with growth hormone may decrease insulin sensitivity, especially at higher doses in susceptible patients. Undiagnosed or untreated hypothyroidism may prevent an optimal response to growth hormone therapy, particularly in children, and it should be monitored. Some products require reconstitution whereas others are available as solutions. A subset of these products is available in prefilled pens or cartridges. In October 2013, there were 29 claims: 48.3% for Nutropin cartridge, 24.1% for Genotropin cartridge, and 10.3% for Nutropin pen. At the last review, a motion for class effect passed unanimously.

MR. RILEY MOVED A CLASS EFFECT. SECONDED BY MR. GREEAR. THE MOTIN PASSED UNANIMOUSLY.

16. Re-Review of Hypoglycemics: TZDs (Green Class)

Ms. Narus gave the Magellan presentation on Hypoglycemics: TZDs. These agents primarily affect fasting glucose. In 2011, the FDA issued a safety announcement stating that using Actos for longer than one year may be associated with an increased risk for bladder cancer. Rosiglitazone (Avandia) based medications were withdrawn from retail pharmacies in November 2011 and are now under a restricted access program. In 2012, the REMS for Pioglitazone (Actos) was removed; however, the Medication Guide was maintained as part of the product labeling. In 2013, the Consensus Panel of the American Association of Clinical Endocrinologists issued a comprehensive algorithm for glycemic control in patients with type 2 diabetes. Alternative monotherapy agents, including GLP receptor agonist, DDP-4 inhibitors, and the EGIs, which offer fewer adverse events or possibly greater benefits compared to TZDs, sulfonylureas, and sodium-dependent cotransporter 2 inhibitors should be used with caution. In October 2013, there were 122 claims: 82.8% for Pioglitazone, 9% for the combination Pioglitazone/Metformin, and 7.4% for Actos. At the last review, a motion for therapeutic alternatives passed unanimously.

DR. LOVE MOVED THE DRUGS IN THE CLASS WERE THERAPEUTIC ALTERNATIVES. SECONDED BY DR. RADER. THE MOTION PASSED UNANIMOUSLY.

After discussion, the committee decided to review all the insulins as a group.

17. Re-Review of Insulins: Long Acting (Green Class)
18. Re-Review of Insulins: Rapid Acting (Green Class)
19. Re-Review of Insulins: Other (Green Class)

Ms. Narus gave the Magellan presentation on Insulins: Long Acting, Rapid Acting, and Other. Long-acting insulins were reviewed. Exogenous insulin products supplement deficient levels of insulin when the body is unable to produce sufficient amounts. Per the American Association of Clinical Endocrinologists and the 2011 Diabetes Care Plan Guideline when insulin therapy is indicated in patients with type 2 diabetes, long-acting basal insulins, particularly insulin analogs, should be the initial choice in most cases due to the lower incidence of hypoglycemia over the NPH products. All insulins can shift potassium from the extracellular to the intercellular space, which should be a reminder caution. In October 2013, there were 500 claims for the long-acting agents: 54.6% for Lanus pen, 36.8% for Lanus vial, 4% for Levemir vial, and 4.6% for Levemir pens. Rapid-acting insulins include insulin aspart, glulisin and lispro. Each of these agents is created by amino acid substitutions at various, unique positions within the native insulin peptide chain. Pharmacokinetics varies among the drugs. Lispro has an onset faster than regular insulin with a duration of three to four hours. Aspart onset is 15 minutes with a duration of three to five hours. Glulisin (Apidra) has an onset of 20 minutes with a duration of 5.3 hours. In October 2013, there were 338 claims for rapid-acting insulins: 34.6% for Novolog pen, 21.3% for Humalog pen, and 21% for Novolog vial. The remaining products include regular insulins, PH, and combinations. In October 2013, there were 71 claims for insulin, others: This was led by the Novolog 70/30 vial and sparse utilization down from there. This class was previously reviewed together. At the last review, a motion for class effect to include at least one formulation from the long-acting, one from the rapid-acting, one from insulin mix, one from insulin 70/30, one from insulin N, and one from insulin R subgroups, and to preferentially include Lantus.

The committee discussed the insulin class as a whole. Dr. Love suggested including pen formulations on the PDL, which would ultimately result in long-term cost savings, decreased adverse events, and better patient compliance. Dr. Demain noted that 61 percent of the prescriptions in the long-acting insulin group were for pens, which were currently non-preferred. Dr. Hope said he did not specifically remember the bidding process for the insulin pens, but he has to abide by the motion. Mr. Greear said he did not remember the conversation last year, but there were concerns with the 500 unit, which is currently preferred. Dr. Hope thought it was a safety concern.

MR. RILEY MOVED A CLASS EFFECT TO INCLUDE AT LEAST ONE FORMULATION FROM THE LONG-ACTING, TO INCLUDE A PEN DELIVERY SYSTEM; ONE FROM THE RAPID-ACTING, TO INCLUDE A PEN DELIVERY SYSEMS; INSULIN MIX; INSULIN 70/30; INSULIN N; AND INSULIN SUBGROUPS; AND PREFERENTIALLY INCLUDING LANTUS. SECONDED BY DR. PHILLIPS. THE MOTION PASSED UNANIMOUSLY.

18. Re-Review of GLP-1 Agonists (Green Class)

Ms. Narus gave the Magellan presentation on GLP-1 Agonists. This subgroup is from the hypoglycemic incretin mimetics and enhancer group, specifically the subgroup of the GLP-1 receptor agonists. Exenatide (Byetta) and Liraglutide (Victoza) are used as an adjunct to diet and exercise in adults with type 2 diabetes. The incretin hormone GLP-1 is part of the system involved in the regulation of glucose homeostasis. Byetta has an added indication of add-on therapy to insulin glargine with or without Metformin and/or a TZD in conjunction with diet and exercise for adults with type 2 diabetes who are not yet achieving glycemic control with insulin glargine alone. Some patients may develop anti-Exenatide antibodies; therefore, attenuation of glycemic response may occur. Exenatide has a black boxed warning regarding the risk of thyroid C-cell tumors and Multiple Endocrine Neoplasia syndrome type 2. Exenatide has been associated with post-marketing reports of acute

pancreatitis including fatal and non-fatal hemorrhagic or necrotizing pancreatitis. Monitoring for pancreatitis following initiations of Exenatide or Liraglutide is necessary. For Liraglutide (Victoza), the Medication Guide should be provided at the start of therapy and with each prescription to advise of the risk of acute pancreatitis and the medullary thyroid carcinoma. In October 2013, there were 33 claims: 57.6% for claims for Victoza, 30.3% for Byetta pens, and 12.1% for Bydureon. At the last review, the GLPs and DPP-4s were combined and it was recommended that they be placed in separate categories. Last year's motion for a class effect passed unanimously.

Dr. Phillips reminded the committee that three physicians requested Victoza be included on the PDL. Victoza also received the most claims. Dr. Demain said it was concerning that the majority of the prescriptions were for medications not on the PDL, and it made one wonder if the needs of the community were being met.

DR. PHILLIPS MOVED A CLASS EFFECT TO INCLUDE VICTOZA. SECONDED BY DR. LOVE. THE MOTION PASSED UNANIMOUSLY.

19. Review Meeting Minutes from November 15, 2013

Dr. Hope said the meeting minutes from November 15, 2013, had not been distributed and would be reviewed at the next meeting.

20. Comments from Committee Members or Chair

Dr. Demain thanked C.J. Kim and Dharma Begich for their many years of service to the committee. He welcomed Robin Cooke and thanked the committee for their hard work. Erin Narus will be joining the committee as a member and not a Magellan representative. The next meeting will be April 18, 2014.

21. Adjourn

Without objection, the meeting adjourned at 10:17 a.m.