ALASKA MEDICAID
PHARMACY AND THERAPEUTICS COMMITTEE

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

FINAL MINUTES OF MEETING
January 18, 2008
8:00 a.m.

Committee Members Present:
Marvin Bergeson, MD
Heidi Brainerd, MS R.Ph
Amber L. Briggs, Pharm.D.
Richard E. Brodsky, MD
Kelly C. Conright, MD
Jeffrey G. Demain, MD
Traci Gale, R.Ph. (telephonic)
Vincent Greear, R.Ph.
R. Duane Hopson, MD
Daniel P. Kiley, DDS, MPH
Diane Liljegren, MD (telephonic)
Andrzej Maciejewski, MD
Gregory R. Polston, MD
Sherrie D. Richey, MD
Trish D. White, R.Ph. (telephonic)

Committee Members Absent:
Marvin Bergeson, MD
Robert H. Carlson, MD
Lucy Curtiss, MD
Janice L. Stables, MSN, ANP

Others Present:
David Campana, R.Ph.
Melinda Sater, Pharm.D, First Health
Alex Malter, MD, HCS

1. Call to Order – Chair

The meeting was called to order at 8:00 a.m.

2. Roll Call

A quorum was present.

3. Public Comment – Local Public/Local Physicians

Dr. Patrick Nolan: Discussed the drug Exenatide, which is currently on the PDL. Exenatide is frequently misunderstood. Endocrinologists use it as a first-line drug, because they do not like to beat up the pancreas with sulfonylureas. Exenatide is effective in many patients, but needs to be reassessed on a regular basis. Some health plans state that Exenatide should not be used in combination with other drugs, including Metformin. However, we do it all the time and it is very effective. Anything that sensitizes the pancreas and can preserve functions is beneficial to patients with type II diabetes.

Exenatide should remain on the PDL. Lantus insulin is used at Providence Hospital and it would be very confusing for the patients if we had to use another insulin. Most endocrinologists believe that Lantus is not interchangeable with other insulins, although there is conflicting data. Levemir may also be acceptable. Both Lantus and Levemir should be included on the PDL. There is currently debate on the use of TZDs. Rosiglitazone has been a good drug, although there is conflicting data with its safety issues. TZDs are reasonably safe as long as the patients are monitored and the black box restrictions are applied. Actos should also be included on the PDL.

Dr. Kevin McGuire: A family practice physician in Anchorage discussed insulins and the preferences of vials versus pens. Pens are a clear advantage across the board due to issues relating to language and culture. Many patients do not like to take out a vial, pull out a needle and put it on the syringe, because it emphasis the fact that they have a disease. The pen is less obtrusive, easier to administer, easier to store, less obvious, and it works very well, especially in younger patients. However, it is necessary to have them both on the PDL so patients do not have to switch between the two.

Dr. Jerry Gitomer: A physician in Anchorage discussed insulins. (Indiscernible – telephonic.) For the ARBs, Diovan is the only drug with a pediatric indication. About 30 percent of Alaskan children that I treat for hypertension with ACE Inhibitors develop a cough. I use quite a bit of angiotensin receptor blockers so it is nice to have a drug with pediatric data. (Indiscernible – telephonic.) I am a fan of combination pills for compliance issues. Many of my patients are on multiple medications so combination pills are very beneficial and should remain on the PDL. (Indiscernible – telephonic.)

4. Review of Benzoyl Peroxide/Clindamycin Combos

There were no public testimonies.

Dr. Sater gave the First Health presentation on Benzoyl Peroxide/Clindamycin Combos. This is a new classification. There is one available fixed-dosed combination and two branded products. The efficacy in the treatment of acne is enhanced by combination therapy. It is particularly useful for inflammatory lesions. There is limited systemic absorption of the Clindamycin component. In November there were 66 claims: 82% for BenzaClin and 18% for Duac. This classification has not been previously discussed and no one wanted to talk about treating acne.

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

5. Review of Renin Inhibitors

Fred Amberger: A representative of Novartis Pharmacueticals discussed Tekturna (Aliskiren). Aliskiren is an orally active direct renin inhibitor that decreases plasma renin activity and inhibits the conversion of angiotensinogen to angiotensin I. In addition, it decreases levels of angiotensin II, which is a powerful vasoconstrictor that contributes to increases in blood pressure. It is indicated for the treatment of hypertension. It may be used alone or in combination with other anti-hypertensive agents. We have studied it both as monotherapy and in combination with other anti-hypertensives. Eight-five to 90% of the BP lowering effect was observed within two weeks of treatment. Studies of ambulatory blood pressure monitoring showed reasonable control throughout the dosing interval. The ratios of mean daytime to mean nighttime blood pressures ranged from .6 to .9. Patients in the placebo

controlled trials continued open label Aliskiren for up to one year. A persistent blood pressure lowering effect was demonstrated by a randomized withdrawal study, which showed a statistically significant difference between patients kept on Aliskiren and those randomized to placebo. Relative to combinations with other anti-hypertensives, Aliskiren has been studied with combinations. Blood pressure reductions with combinations were greater than with the corresponding monotherapy. Aliskiren has been evaluated for safety in more than 6,460 patients, including over 1,740 patients that were treated for longer than six months and more than 1,250 patients that were treated for more than one year. In the placebo controlled clinical trials, discontinuation of therapy due to clinical adverse events occurred in 2.2 percent of patients treated with Aliskiren versus 3.5 percent of patients given placebo. In controlled clinical trials, clinically relevant changes in standard laboratory parameters were rarely associated with the administration of Aliskiren.

Dr. Sater gave the First Health presentation on Renin Inhibitors. This is a new classification. Tekturna, the only drug in the class, targets the conversion of angiotensinogen to angiotensin I. It is a direct renin inhibitors. It is FDA approved for the treatment of hypertension. The P-450 pathway also metabolizes it so there are some significant drug interactions. There is no outcomes data, but it was generally well tolerated in clinical trials. In November there were 13 claims, all for Tekturna. Since this is a new class, there was no previous discussion and no physicians wanted to talk about this drug.

Dr. Maciejewski said Tekturna was new on the market, but he was very enthusiastic about the agent. It is more potent than the other renin blocking agents. If a patient misses a dose, nothing will happen because the lowering blood pressure effect is maintained for almost a week. Tekturna is also doing very well with combinations. It is a new drug so the use in clinical practice is minimal. However, this drug should be considered as a first-line agent due to its mechanism of action.

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

6. Re-review of ACE Inhibitors

There were no public testimonies.

Dr. Sater gave the First Health presentation on ACE Inhibitors. There are 10 available products in this class. All are FDA approved for the treatment of hypertension and may be indicated for initial therapy if compelling indications exist. Perindopril, Trandolapril and Ramipril are not available in combination with hydrochlorothiazide, although the others are. They have similar clinical efficacy and adverse drug reaction profiles. OHSU information states that they are equivalent. In November there were 1,507 claims, including the combination products: 84% for Lisinopril, 8% for Enalapril, and the rest was divided equally among the others. The currently preferred agents are Lisinopril, Enalapril, Benazepril, Captopril, Lisinopril hydrochlorothiazide combination, and Benazepril hydrochlorothiazide combination. At the last review, the half-life and subtle differences between the agents was discussed. The motion for a class effect, preferentially including Lisinopril, passed unanimously. Since the last review, Altace has introduced a tablet formulation and generic Ramipril capsules have been introduced to the market. No physicians wanted to talk about ACE Inhibitors.

DR. DEMAIN MOVED A CLASS EFFECT, PREFERENTIALLY INCLUDING LISINOPRIL ON THE PDL. SECONDED BY DR. MACIEJEWSKI. THE MOTION PASSED UNANIMOUSLY.

7. Re-review of Angiotensin II Receptor Blockers (ARBs)

Fred Amberger: A representative of Novartis discussed Exforge, a combination product of Diovan and Amlodipine. Hypertension continues to be a challenge to successfully control. Currently only 37% of patients with hypertension are at goal. A number of clinical trials have demonstrated that most hypertensive patients need two or three drugs to get to goal. Studies have shown that as patients take longer to get to goal the discontinuation rate increases due to changes in their therapy. It is a fixed-dose combination of Amlodipine and Diovan. By complimentary mechanisms, Amlodipine and Valsartan lower peripheral resistance thereby lowering blood pressure. It is indicated for the treatment of hypertension, however the fixed-dose combination is not indicated for the initial therapy. In double blind, placebo controlled trials, blood pressure reductions were significantly greater with it than with Amlodipine or Valsartan alone. Blood pressure goals of less than 140/90 were achieved by 73 patients treated with Exforge 10/320 and 26% of patients with placebo. Blood pressure control rates, defined as less than 130/80, with Exforge 10/320, when compared to placebo, were as follows: in patients with stage I hypertension 49% reached goal versus 6% on placebo; in patients with stage II hypertension 20% reached goal versus 3% on placebo; and in hypertensive patients 65 years and older, 33% reached goals versus 3% on placebo. Relative to the adverse event profile, it has been evaluated for safety in over 2,600 patients with hypertension. Over 1,440 of these patients were treated for at least six months and over 540 were treated for at least one year. Adverse experiences have generally been mild and transient in nature and have only infrequently required discontinuation of therapy. The overall frequency of adverse experiences was neither dose related or related to gender, age or race.

Derek Terada: A representative of Boehrnger Ingelheim discussed Telmisartan (Micardis). A large-scale clinical trial, including 1,600 patients with stage I and stage II hypertension, was discussed. The patients were either started on, or switched to, Micardis. After having their medications titrated, their office blood pressures were greater than 140/85. At the end of the 10-week study, Micardis produced ambulatory blood pressure reductions of 10% that corresponded to an office blood pressure reduction by cuff of 22/12. The patients that were on another drug and then switched to Micardis had an ambulatory blood pressure reduction of 8/5, which translated to additional blood pressure reductions of 17/10. Micardis is being evaluated for cardiovascular outcomes in three ongoing global trials.

Jason Alm: A representative of Daiichi Sankyo discussed Olmesartan (Benicar). Benicar is used as first-line therapy either alone or in combination with other anti-hypertensive agents. In an analysis of seven clinical trials in 2,600 patients with stage II hypertension, Benicar at 20 and 40 milligrams significantly reduced blood pressure of about 15/12 and 17/13, respectively. The withdrawal rate due to adverse events, as well as the incidence of adverse events, was similar to that of placebo. The only adverse event that occurred more frequently with Benicar versus placebo was dizziness at 3% versus 1%. Benicar is also available in combination with hydrochlorothiazide as Benicar HZT. It is available in doses of 20-12.5, 40-12.5, and 40-25. Benicar HZT is also indicated for the treatment of hypertension, but it is not indicated for first-line therapy. The incidence of adverse events and withdrawal rates with Benicar HZT were similar to placebo. Several trials and their results were discussed.

Tammy Egger: A representative of Bristol-Myers Squibb discussed Irbesartan (Avalide) and Irbesartan (Avapro). (Indiscernible – telephonic.)

Kate Ryan: A representative for AstraZeneca discussed Candesartan (Atacand). Atacand has two indications: hypertension and congestive heart failure. It is indicated for the treatment of hypertension and may be used alone or in combination. All of the ARBs have blood pressure lowering abilities. Atacand has demonstrated similar efficacy, but it has greater efficacy in reducing diastolic blood pressure compared to Losartan. Atacand also has an indication for congestive heart failure. It has an added effect when used with ACE Inhibitors. The CHARM trial, which evaluated the use of Atacand in patients with chronic heart failure, was reviewed. (Indiscernible – telephonic.)

Dr. Sater gave the First Health presentation on Angiotensin II Receptor Blockers (ARBs). There are seven available products. The indications vary by product. They have similar pharmacokinetic profiles and clinical efficacy. All drugs in the class have combination products with hydrochlorothiazide and two now have combination products with Amlodipine. No drug in this class is available generically. Diovan, Cozaar, Benicar, Micardis, Avapro and the corresponding hydrochlorothiazide combinations are currently preferred. In November there were 748 claims, including the combination products: 41% for Diovan, 27% for Cozaar, 12% for Benicar, and less than 20% for the combinations. At the last review there was a lengthy discussion on the meaning of class effect and for which indications class effect was appropriate. The motion to declare a class effect carried with one opposed. There have been no significant changes in this class since the last review. Dr. Leslie Glasgow supports Avapro and Avalide due to preserved renal function and good hypertension control in renal patients.

Dr. Maciejewski said clinical studies and FDA approval is based on clinical results. Different drugs have different indications and the data indicates that there is not a class effect.

Dr. Brodsky noted that FDA approval was based on studies. Many of the drugs in the class probably work, but have not been studied enough to obtain FDA approval. There are exceptions and times when a drug clearly works or does not work. There have been studies that showed a drug works and then a later study that showed it did not work at all. There have been recent articles published on the FDA and problems with their approval process.

Dr. Maciejewski pointed out that Cozaar had made two attempts to get an approval for a heart failure indication and failed both times.

DR. CONRIGHT MOVED A CLASS EFFECT. SECONDED BY DR. POLSTON. THE MOTION PASSED WITH ONE OPPOSED.

8. Re-review of Calcium Channel Blockers (CCBs)

Jason Alm: A representative of Daiichi Sankyo discussed Azor, a fixed-dose combination of Amlodipine and Olmesartan. It is indicated for the treatment of hypertension either alone or in combination with other antihypertensive agents. However, it is not indicated for initial antihypertensive therapy. A multi-center, randomized, double blind, placebo trial that evaluated both the efficacy and safety of the combination of Amlodipine and Olmesartan, as compared to the respective monotherapy components, was reviewed. The results show that each of the combinations had significantly greater reductions in both diastolic and systolic blood pressure compared to their

monotherapy components. The hypertensive efficacy of Azor was similar with African-American patients, diabetics, patients with stage II hypertension, and elderly patients. Reported adverse events were generally mild and seldom led to discontinuation. Edema was the most common drug related adverse event and was experienced in a total of 14.3% of the patient population. Edema was proactively assessed and as a result the observed incidents were higher than that reported in product labeling for Norvasc and Benicar.

Dr. Sater gave the First Health presentation on Calcium Channel Blockers (CCBs). There are nine available chemical entities. The dihydropyridine group, specifically Amlodipine, is also available in combinations with ACE Inhibitors, Angiotensin Receptor Blockers, and Atorvastatin. All are indicated for the treatment of hypertension, except Nimodipine. Others have indications for angina, but all the drugs in the class are used for all indications, except for Nimodipine. Amlodipine is the only agent that can be crushed without altering the once daily dosage regimen. Oregon Health Sciences University found no significant differences between the agents in this class. Generic Diltiazem, generic Verapamil and a couple of branded products are currently preferred in the nondihydropyridine group. In November, in the nondihydropyridine group, there were 194 claims: 54% for extended release Diltiazem, 27% for generic Verapamil, and less than 20% for the rest of the branded generic products put together. Generic Nifedipine, Norvasc, generic Felodipine, a couple of branded Nifedipine products, Dynacirc and Sular are preferred in the dihydropyridines group. In November, for the dihydropyridine group, there were 503 claims: 82% for generic Amlodipine, 9% for extended release Nifedipine, and less than 10% for the other drugs combined. In the previous discussion there was a brief review of the advantages of Amlodipine over the other drugs in this class and the need for both dihydropyridines and nondihydropyridines on the PDL. The motion for a class effect when treating hypertension, including at least one Amlodipine, one Verapamil, and one Diltiazem product, passed unanimously.

Dr. Demain said Amlodipine was the only dihydropyridine product approved for children.

DR. CONRIGHT MOVED A CLASS EFFECT WHEN TREATING HYPERTENSION, AND TO INCLUDE AT LEAST ONE AMLODIPINE, ONE VERAPAMIL, AND ONE DILTIAZEM PRODUCT ON THE PDL. SECONDED BY DR. DEMAIN. THE MOTION PASSED UNANIMOUSLY.

9. Re-review of Topical Immunomodulators

Leigh Platte: A representative of Astellas discussed Tacrolimus (Protopic). Tacrolimus is indicated as second-line therapy for short-term or non-continuous, long-term treatment of moderate to severe atopic dermatitis in non-immunocompromised patients who have failed first-line therapy. It is not indicated for children under the age of 2. The dosage for children ages 2 to 15 is .03% and for adults it is .1%. In over 2 million patients that have been treated in the United States and 5.5 million patients treated worldwide, it is clinically studied in over 20,000 patients, of which 8,000 or more were children. There are currently 8,750 patients in long-term follow-up. There have been 23 comparative trials and no reports of malignancy, but we do have a black box warning. Several studies were discussed. The safety and efficacy of Tacrolimus has been demonstrated in numerous short- and long-term trials. No evidence of a causal link between the use of Tacrolimus ointment and the rare cases of skin cancer has been reported. The safety profile of Tacrolimus, coupled with its demonstrated efficacy, makes it a very important tool in the treatment of children and adults.

Dr. Sater gave the First Health presentation on Topical Immunomodulators. There are two available agents in this class. Both are currently preferred. The indications differ slightly between agents. Both carry pediatric indications. Protopic has a lower strength for pediatric dosing. Systemic absorption is considered clinically insignificant for both agents. The adverse drug reaction profiles are similar. Both products carry black box warnings regarding cancers. The dosage forms differ. Elidel is a cream and Protopic is an ointment. Other dosage forms are under investigation by the companies. In November there were 114 claims: 68% for Elidel and 32% for Protopic. There was limited discussion at the last review regarding the preference of Elidel in pediatrics due to the fact that it stings a little bit less. The motion to include both agents on the PDL passed unanimously.

Dr. Demain felt both of the drugs should be included on the PDL. The FDA box warning noted that these drugs were being used outside of the guidelines. The guidelines indicate that Elidel should be used for mild to moderate eczema while Protopic should be used for moderate to severe eczema. Even though they are similar, they have different indications based on the severity of the eczema.

The committee discussed the number of patients who had mild to moderate eczema as compared to moderate to severe eczema.

DR. DEMAIN MOVED A CLASS EFFECT WITH BOTH PRODUCTS PREFERRED. SECONDED BY DR. MACIEJEWSKI.

The committee discussed whether it was necessary to include both products on the PDL as opposed to simply declaring a class effect and utilizing the medically necessary clause. Dr. Demain felt it was necessary to include both, because of the even split between patients with mild to moderate and moderate to severe eczema. The committee further discussed the motion.

THE MOTION FAILED WITH SEVEN OPPOSED.

DR. LILJEGREN MOVED A CLASS EFFECT WITH ELIDEL PREFERRED. THERE WAS NO SECOND.

DR. KILEY MOVED A CLASS EFFECT. SECONDED BY DR. BRIGGS. THE MOTION PASSED WITH FIVE OPPOSED.

10. Re-review of Oral Beta-Blockers

Long Nguyen: A representative of GlaxoSmithKline discussed Coreg CR. Beta-blockers have come a long way from being contraindicated to becoming the standard of care in heart failure. There is data available that beta-blockers are no longer a class effect. Coreg has the most data available and shows the greatest benefit in reduction in mortality, as well as cardiovascular events. In 2006, Coreg CR was approved based on the fact that compliance was an issue with heart failure patients. As of today, there is no data or study that has looked at Coreg CR compared to generic, twice a day Carvedilol. With limited or no data available, switching patients from Coreg CR to generic Carvedilol is not recommended and may put patients at risk for cardiovascular events and even death. Therefore, Coreg CR should remain on the PDL.

Jake Knee: A representative of Forest Labs discussed Bystolic, which is a new product that just received FDA approval in December. Beta-blockers are the fourth largest drug class prescribed in America and it continues to grow. Beta-blockers have long been, and continue to be, the drug of choice in treating hypertension. However, due to certain side effects, there have been populations that do not respond well and/or cannot tolerate beta-blockers. The common side effects of beta-blockers include fatigue, erectile dysfunction, cold extremities, hyperactivity, airway disorder, and depression. In addition to these adverse events, efficacy and safety limitations exist in African Americans, obese and diabetic patients. Bystolic is the next generation of beta-blockers with a unique mechanism of action. In contrast to traditional beta-blockers, Bystolic actually decreases PVR while increasing stroke volume and maintaining cardiac output. Bystolic is indicated for, and delivers, significant blood pressure reductions as monotherapy or in combination. More importantly and uniquely, Bystolic offers blood pressure reductions across the broad range of general populations, as well as the special populations like African American, obese and elderly patients. Bystolic has a tolerability profile similar to placebo. The most commonly reported adverse events did not separate from placebo. Dropout rates due to adverse events with Bystolic were 2.8% in the package insert as opposed to 2.2% with placebo. Bystolic has been extensively studied worldwide for over 10 years in 10 million patients. There have been a billion doses administered worldwide. There is a wealth of clinical data with 72 clinical trials in 6,500 patients. There are no contraindications for people with asthma, because it does not have any action on the beta-2.

Dr. Sater gave the First Health presentation on Oral Beta-Blockers. There are 14 available entities in this class. Indications vary between agents. Some have beta selectivity while others do not. Carvedilol and Labetalol have alpha-1 receptor activity in addition. Currently the preferred agents are: Atenolol, Propranolol, generic Lopressor, Coreg CR, Nadolol, Coreg, Labetalol, Bisoprolol, Sotalol, Acebutolol, and Betaxolol. In November there were 1,646 claims: 43% for Atenolol, 11% for Propranolol, 11% for generic Toprol XL, 10% for generic Lopressor, 6% for generic Coreg, 5.5% for Toprol XL, 4% for Coreg CR, and less than 10% for all the rest. In previous discussions, the therapeutic benefit of Carvedilol over the other agents was discussed. The motion to include Carvedilol and Coreg CR, and include a mix of beta-1 selective and non-selective agents, passed with two opposed. There was much support from the Alaska Heart Institute for the inclusion of Coreg and Coreg CR on the PDL.

Dr. Brodsky noted that the most recent guidelines published by the American College of Cardiology and the American Heart Association do not recommend one beta-blocker for heart failure, but three: Bisoprolol, Carvedilol, and Metoprolol.

Dr. Maciejewski noted that some beta-blockers had completely different properties. Metabolic effects were discussed. The classic selective and non-selection beta-blockers have negative effects on metabolic such as weight gain, lipid profile, and insulin resistance whereas Bystolic and Carvedilol do not have negative metabolic effects. Bystolic and Carvedilol work differently, so you cannot even consider them equivalent.

Dr. Demain referenced the adverse effects section in the informational packet. When comparing Carvedilol to Metoprolol, Carvedilol has a significant side effect profile as compared to Metoprolol.

Dr. Maciejewski discussed the side effect profiles. Cardiologists feel that Metoprolol is more efficacious due to weight control and heart irritability issues.

An unidentified female made several comments over the telephone regarding the difference between the beta-blockers, which could not be heard on the tape.

Dr. Brodsky pointed out that this was a very diverse classification and many of the drugs had different indications and side effects. The generic drugs would probably be included on the PDL.

Dr. Demain pointed out that you could not assume all the generic drugs would be included on the PDL.

DR. DEMAIN MOVED TO INCLUDE AT LEAST ONE OF BISOPROLOL, CARVEDILOL OR METOPROLOL ON THE PDL; A SHORT-ACTING PROPRANOLOL AND ATENOLOL; WITH THE REMAINDER BEING A CLASS EFFECT. THERE WAS NO SECOND.

Dr. Maciejewski advocated for the new agent Bystolic, which the motion would exclude. There is also a difference between selective and non-selection agents. Metabolic issues are not addressed and there is concern about the effect beta-blockers are having on Metabolic Syndrome, which is becoming an epidemic in this country. The motion should be amended to include the two metabolically safe agents.

DR. MACIEJEWSKI MOVED TO INCLUDE BYSTOLIC, COREG, COREG CR, AND THE GENERIC BETA-BLOCKERS THAT ARE ALREADY ON THE PDL. THERE WAS NO SECOND.

DR. CONRIGHT MOVED THAT THERE BE AT LEAST ONE MEDICATION THAT IS SHORT- AND LONG-ACTING WITH AN INDICATION FOR HEART FAILURE. THERE WAS NO SECOND.

DR. BRIGGS MOVED A CLASS EFFECT TO INCLUDE BISOPROLOL, A CARVEDILOL PRODUCT, METOPROLOL, AND METOPROLOL SUCCINATE. THERE WAS NO SECOND.

The committee discussed the motion. Dr. Maciejewski noted that this motion would not include a selective beta-blocker that had no metabolic effects. (Several discussions not on the microphone.)

DR. MACIEJEWSKI MOVED TO FOLLOW THE RECOMMENDATIONS OF THE AMERICAN COLLEGE OF CARDIOLOGY AND INCLUDE CARVEDILOL, BISOPROLOL, AND METOPROLOL, AS WELL AS BYSTOLIC, ON THE PDL. THERE WAS NO SECOND.

Ms. Brainerd pointed out that the motions were focusing on heart failure, but beta-blockers were used for many different indications. The committee agrees that they are not all the same. She agreed with Dr. Liljegren that Sotalol should be have been separated out. The medical necessity clause can always be utilized.

MS. BRAINERD MOVED A CLASS EFFECT. SECONDED BY DR. BRIGGS.

Dr. Conright expressed concern about the motion. If the language specifically includes a drug with heart failure indications, those drugs also have hypertensive indications; whereas if the motion is for a class effect, we could get a drug that does not heart failure indications.

Dr. Briggs said the committee was often concerned with what may or may not make it onto the PDL. We want to insure that our patients are treated appropriately, but we also are looking for cost savings. If we declare a class effect, we can see what happens and learn from it in our next review. We always have the opportunity to write medically necessary.

THE MOTION PASSED WITH TWO OPPOSED.

DR. MACIEJEWSKI MOVED TO ADD BYSTOLIC AND CARVEDILOL TO THE PDL WITH THE UNDERSTANDING THAT THEY ARE NOT A CLASS EFFECT. SECONDED BY DR. DEMAIN.

The committee discussed the motion. Dr. Brodsky urged the committee to vote against the motion. Bystolic is a new and expensive drug. The medically necessary clause can always be utilized. Dr. Maciejewski pointed out that using a better drug would actually be cheaper for the state in the long run and they were not that expensive. Dr. Conright asked why Carvedilol should be on the PDL as opposed to any drug that has an indication for heart failure. Dr. Maciejewski said the drugs differed in their mechanism of action.

THE MOTION FAILED WITH NINE OPPOSED.

11. Re-review of Sulfonylureas

There were no public testimonies.

Dr. Sater gave the First Health presentation on Sulfonylureas. There are three entities in this class. There were absolutely no changes since the last review. At the last review, there was a short discussion regarding the subtle differences between the agents and the need for both immediate release and extended release products. The motion for a class effect, both an ER and IR product, passed unanimously. The currently preferred products are Glyburide, Glipizide ER, Glipizide, Glimepiride, and Micronase Glyburide. In November there were 373 claims.

DR. LILJEGREN MOVED A CLASS EFFECT, TO INCLUDE AT LEAST ONE SHORT-ACTING AND ONE LONG-ACTING PREPARATION ON THE PDL. SECONDED BY DR. DEMAIN.

Dr. Conright noted that Glipizide was the preferred agent for elderly patients due to its shorter half-life and should be included on the PDL.

DR. CONRIGHT MOVED TO AMEND THE MOTION TO INCLUDE A GLIPIZIDE PRODUCT ON THE PDL. SECONDED BY DR. MACIEJEWSKI. THE AMENDMENT PASSED UNANIMOUSLY.

THE MOTION, AS AMENDED, PASSED UNANIMOUSLY.

12. Re-review of Insulins

Matt Kresken: A representative of Sanofi Aventis discussed Lantus and Apidra. Lantus has over six years of clinical experience with over 200 studies utilizing Lantus once daily to support its safety and efficacy. It is the most prescribed insulin on the market today, because of its predictability and ease of use. Lantus should be maintained on the PDL, because it is not interchangeable with other insulins. It is the only basal insulin designed to mimic normal physiologic insulin secretion. It demonstrates a relatively constant concentration over 24 hours. In the Treat to Target study, 59% of patients were able to achieve an A1C of less than 7% when Lantus was added to oral insulins and actively titrated. Several studies were discussed. A study recently presented at an International Diabetes meeting showed Lantus providing superior A1C reduction while using less insulin than Detemir. Data from the State of Iowa shows that Medicaid patients on Lantus who were switched to Detemir showed a loss of glycemic control of almost 1% over six months, they used higher doses, and had more weight gain. Lantus is the only insulin analog FDA approved solely for once daily dosing. It has been on the market for over six years and has over 200 published clinical trials. The primary care community does not consider Lantus to be interchangeable with any other insulins. Apidra is a rapid acting insulin. It has been shown to have a more rapid onset of action than Lispro across all BMIs, as well as fewer unexplained hyperglycemic episodes. It is the only rapid acting agent to have specific data on post-meal dosing in order to more accurately match food intake.

Christian Herter: A representative of Novo Nordisk discussed (Levemir) Detemir. It is a long-acting insulin analog based on human regular insulin. Its duration of action is pretty much the same as the other analog Glargine. With its long duration of action, Detemir has been shown to be effective for managing type II diabetes using a single dose in the evening before bedtime. In our phase III clinical trials, we have shown that there has been less weight gain with Levemir compared with the other insulins. In a large, multicenter, observational trial of 511 patients there was actually weight loss despite a hemoglobin A1C improvement. Levemir has a unique mechanism of action and structure. It is based on human regular insulin that has been modified through the addition of muristic acid, which is the principal constituent of avocado oil. This changes the charge in the molecule so that the Levemir molecules attract and adhere to each other, which accounts for its long duration. A paper published in Diabetes Care in 2004 showed that the glucose lowering effect of Levemir was much more predictable than any of the other insulins. Several studies on the dosing of Levemir were discussed.

Rick Smile: A representative from Eli Lilly discussed the Humalog family of insulins. Lispro is an insulin analog indicated for the control of hyperglycemia in patients with diabetes. Through rapid acting, it was not only approved for general use in patients with diabetes, but also for special populations such as children as young as 3 years of age and patients older than 65 years of age. Treatment with Humalog results in a lower prostpranal glucose level than regular insulin and a lower occurrence of nocturnal hyperglycemia. Because it can be injected immediately before meals, it enhances lifestyles and compliance. Lispro can be used with newer methods of administration such as continuous subcutaneous insulin infusion or pre-filled insulin pens. The pre-filled insulin pens are a convenient and reliable form of insulin delivery with a high patient preference rating and acceptable safety profile. Lispro demonstrated a positive effect on the quality of life for all patients with diabetes without affecting healthcare costs. Lispro was associated with high patient acceptance in reports of hyperglycemia. It has also been shown to provide more treatment flexibility and satisfaction. Humalog Mix 75/25 is the pre-mixed insulin indicated for the treatment of patients with diabetes. Lispro has been shown to have faster absorption, faster onset of action, and a shorter duration of action than regular human insulin after subcutaneous administration. Several studies were discussed. Clinical studies have been conducted to compare the safety and efficacy of Humalog Mix 75/25 to Lantus in

patients with type II diabetes. The Humalog family of insulins should be included on the PDL to provide an additional means for the practitioners of Alaska to gain control of this worldwide epidemic called diabetes.

Dr. Sater gave the First Health presentation on Insulins. There are six types of insulins for consideration. There are three recombinant DNA and three biosynthetic analog groups that were considered by the committee last year. There are short intermediate acting and pre-mixed combinations in the recombinant arm; and rapid, long, and pre-mixed combinations in the biosynthetic group. In November there were 638 claims for all types of insulins. In the long-acting biosynthetic group, Lantus and Levemir are preferred and Lantus vials had 86% of the claims. In the short-acting biosynthetic group, Novolog is the preferred agent and received 61% of the claims. In the biosynthetic pre-mixed combination group, Novolog Mix 70/30 received 78% of the claims. In the short-acting recombinant insulin group, Novolin R is the preferred agent and received 88% of the claims. In the intermediate-acting recombinant insulin group, Novolin N is the preferred agent and received 80% of the claims. In the pre-mixed recombinant group, Novolin 70/30 is the preferred agent and received 93% of the claims. At the last review there was a significant discussion of the Grandfather Clause and the importance of brand stability. Each subclass was considered separately. The need for products in each subclass was agreed upon. The motion to declare a class effect in each distinct subclass and to grandfather patients currently using Lantus, if it was not preferred, passed unanimously. Inhaled insulin was considered separately, although that is no longer a concern as Exubera was removed from the market. Dr. Koval primarily uses Lantus for her patients requiring long-acting insulin. However, she likes the differences between the pens and the vials. She likes the pens for her short-acting insulin patients and vials for her long-acting patients. The pens make it easier for the patients to carry their medications with them and they reduce the possibility of a medication error being made by the patient.

DR. CONRIGHT MOVED A CLASS EFFECT IN EACH DISTINCT SUBCLASS AND TO GRANDFATHER PATIENTS CURRENTLY USING LANTUS IF IT IS NOT PREFERRED. SECONDED BY DR. DEMAIN. THE MOTION PASSED UNANIMOUSLY.

13. Re-review of Hypoglycemics, Thiazolidinediones (TZDs)

Gene Felber: A representative of Takeda discussed Actos. Safety data from proactive studies that incorporated into the adverse events warning section of Actos prescribing information was done in February 2007. The overall safety and tolerability was consistent with known adverse events. Compared to placebo, slightly more patients in the Actos group were hospitalized with heart failure: 4% with placebo versus 5.7% in the Actos group. The incidence of death subsequent to report of serious heart failure was 1.5% in Actos versus 1.4% in placebo. Several new studies have been recently published, which will not be reviewed, but any questions will be answered. In August 2007 black box warnings added to product information of Actos and the combination product regarding CHF placed certain important information from the previous Actos label in a more prominent position. Actos is contraindicated in patients with NYHA class III and IV heart failure. There is not a black box warning, but added to the label there is the added risk of fracture in female patients receiving Actos. It is not seen in males and we are still investigating the mechanism of action.

Rob Pearson: A representative of GlaxoSmithKline discussed Avandia. Recently the FDA has performed meta-analyses of short-term trials with Avandia with a mean duration of six months. In the analyses, they observed an increased risk of myocardial ischemic events with Avandia compared to

placebo, but there was no observation of increased risk with Avandia compared to Metformin or the sulfonylureas. These findings have now been added to the labeling information for Avandia. There have been three large, U.S. managed care databases and studies performed with over 1.3 million patients. The risk of myocardial infarction among Avandia patients was found to be similar to that of the other oral anti-diabetic agents. Several trials have demonstrated no increased risk for myocardial ischemic events with Avandia compared to the control arms. There are four large, ongoing trials currently being conducted. The Data Safety Monitoring Boards for each of these trials have all voted to proceed with the studies as planned based on the safety information during those reviews. The FDA recently stated that to date no oral anti-diabetic drug has been conclusively shown to reduce cardiovascular risk. Avandia has been proven to reduce insulin resistance and slow the progression of beta-cell dysfunction. Avandia remains the most studied oral anti-diabetic agent and has been proven to sustain glycemic control for up to five years. Avandia should remain accessible to Alaska patients while we awaiting definitive data from the ongoing long-term prospective trials.

Dr. Sater gave the First Health presentation on Hypoglycemics, Thiazolidinediones (TZDs). There are two TZDs currently available. Both are available in combination with Metformin and Glimepiride. Both have similar adverse drug reaction profiles and efficacy. There are a variety of indications. Both of the agents are currently preferred. In November there were 438 claims, including the combinations: 80% for Actos, 15% for Avandia, and 5% for the combinations. Without discussion, a motion for a class effect passed unanimously last year. Since the last review, a number of safety concerns have been raised about TZDs. The package insert has been changed across the class with box warnings. Dr. Koval has very few patients still on TZDs as most of her patients have serious heart disease. She has some concerns about the safety of the drugs in this class.

DR. CONRIGHT MOVED A CLASS EFFECT. SECONDED BY DR. MACIEJEWSKI.

Ms. Brainerd felt the committee should carefully watch the results of further review on this class of drugs and re-review the class as needed.

THE MOTION PASSED WITH ONE OPPOSED.

14. Re-review of Hypoglycemics, Metformins (Biguanides)

There were no public testimonies.

Dr. Sater gave the First Health presentation on Hypoglycemics, Metformins (Biguanides). There is one available entity with several formulations, both immediate release and extended release. Combinations are available with Glipizide and Glyburide. Indications vary a little bit between the formulations. Generic Metformin immediate release and extended release are the preferred agents in this class. In November there were 862 claims: 83% for immediate release Metformin and 12% for extended release Metformin. At the last review, the importance of having both an extended and immediate release formulation was discussed. A class effect was declared. A motion to include both immediate and extended release tablets carried unanimously.

DR. CONRIGHT MOVED A CLASS EFFECT WITH AN IMMEDIATE RELEASE AND EXTENDED RELEASE PRODUCT BEING INCLUDED ON THE PDL. SECONDED BY DR. MACIEJEWSKI. THE MOTION PASSED UNANIMOUSLY.

15. Re-review of Hypoglycemics, Metglinides

There were no public testimonies.

Dr. Sater gave the First Health presentation of Hypoglycemics, Meglitinides. There have been no changes in this class since the last review. There are two available agents, Prandin and Starlix. Both are preferred. In November there were 7 claims: 6 for Starlix and 1 for Prandin. There was no discussion at the last review. A class effect was declared and the motion carried unanimously. Dr. Koval uses Prandin. She finds it useful in early diabetes and savvy patients can self-titrate.

DR. CONRIGHT MOVED A CLASS EFFECT. SECONDED BY DR. MACIEJEWSKI. THE MOTION PASSED UNANIMOUSLY.

16. Re-review of Hypoglycemics, Incretin Enhancers/Mimetics

Jesse Hong: A representative Amylin Pharmaceuticals discussed Byetta and Symlin. Byetta improves glycemic control through multiple actions. It enhances glucose dependent insulin secretions, restores first-base insulin response, suppresses inappropriately elevated glucagon secretions, reduces food intake, and (indiscernible). These combined actions cause a significant A1C reduction, as well as progressive weight reduction and improvement of cardiovascular risk over long-term treatment. We have recently published our three-year clinical trial results. The trial shows that the patients continue to experience continuous A1C reductions and weight loss over three years. Unlike the other diabetes therapies that are associated with weight gain or weight neutral, the significant and progressive reduction of body weight is a distinct treatment benefit of Byetta therapy. Weight loss, coupled with consistent A1C reduction, makes patients using Byetta feel better about themselves. Symlin is an adjunct therapy for type I and type II diabetic patients who use mealtime insulin therapy and have failed to achieve desired glucose control.

Dr. Sater gave the First Health presentation on Hypoglycemics, Incretin Enhancers/Mimetics. There are three entities in this class. One is available in combination with Metformin. Two products are injections and one is oral. The mechanisms are slightly different. All agents are preferred. In November there were 94 claims: 75% for Januvia, 21% for Byetta, and 6% for Janumet and Symlin. At the last review there was limited discussion on the necessity of having all tools available to treat diabetes. The motion to prefer all drugs passed unanimously. Since the last review there has been a pancreas warning associated with Byetta. Dr. Koval said all the agents have unique and somewhat different roles in the treatment of diabetes and would like to see all of the drugs preferred.

Mr. Campana said Byetta required prior authorization, because initially there was a concern about using it only for weight loss and not for the treatment of diabetes. This may no longer be a concern. An alternative to the prior authorization is a step edit that would look for Metformin or another sulfonylurea before allowing the prescription for Byetta to be filled.

In response to Dr. Malter, Dr. Sater pointed out that not every trial was included in the informational packet. The weight loss referred to for Byetta was in an early trial.

Dr. Conright said physicians did not have to worry about hyperglycemia with Januvia and it clearly has a different mechanism of action. She asked if there were significant differences between Byetta and Symlin. She felt the committee should consider separating out Januvia.

Dr. Sater said all the drugs had different mechanisms. Symlin is only indicated for patients who are using insulin whereas Byetta can be used for patients who are still taking oral therapy.

Dr. Briggs said although Byetta is not indicated for use with insulin, patients have used it with insulin with success.

The committee discussed the fact that Symlin was not used very often. Dr. Maciejewski said he used Symlin. He did not believe that physicians realized all the advantages of using Symlin and felt it was a very important drug.

DR. LILJEGREN MOVED BYETTA, SYMLIN AND JANUVIA BE PREFERRED, BUT JANUMET NOT BE SPECIFICALLY PREFERRED. SECONDED BY DR. MACIEJEWSKI. THE MOTION PASSED WITH THREE OPPOSED.

17. Re-review of Alpha-Glucosidase Inhibitors

There were no public testimonies.

Dr. Sater gave the First Health presentation on Alpha-Glucosidase Inhibitors. There are two available products. The indications vary. They have similar pharmacokinetic profiles and clinical efficacy. Typically they do not cause hyperglycemia. Precose is the preferred agent. In November there were 10 claims: 100% for Precose. There was no discussion at the last review. The motion for class effect passed unanimously. Dr. Koval feels the drugs are equivalent.

DR. CONRIGHT MOVED A CLASS EFFECT. SECONDED BY DR. MACIEJEWSKI. THE MOTION PASSED UNANIMOUSLY.

18. Re-review of Glaucoma Agents

There were no public testimonies.

Dr. Sater gave the First Health presentation on Glaucoma Agents. Last year we considered all of these classes separately. There have been no changes in any of these classes since the last review. In the ophthalmic agonists group, both agents are preferred. In November there were 9 claims, all for Alphagan P. In the ophthalmic beta-blockers group, Timolol, Carteolol, Levobunolol, Timolol gel solution, and Betoptic S are preferred. In November there were 10 claims: 40% for Timolol gel solution, 20% for Carteolol. There was no discussion at the last review. The motion for a class effect passed unanimously. Nothing is new in that class. For Carbnic Anhydrase Inhibitors group, all three agents are preferred. In November there were 5 claims, all for Cosopt. The motion for a class effect passed unanimously. Nothing is new in that group. All the Prostaglandin agents are preferred. In November there were 33 claims: 55% for Xalatan, 36% for Travatan, and 9% for Lumigan. Xalatan has a lot of local support. The motion for a class effect, preferentially including Xalatan, passed with two opposed.

DR. DEMAIN MOVED A CLASS EFFECT FOR ALL THE GROUPS, PREFERENTIALLY INCLUDING XALATAN IN THE PROSTAGLANDIN ANALOG GROUP. SECONDED BY DR. CONRIGHT. THE MOTION PASSED WITH ONE OPPOSED.

Dr. Demain revisited the beta-blockers. The motion was for a class effect, although we did not specifically identify one of the three drugs that have been recognized and approved by the American College of Cardiology and American Heart Association for the treatment of heart failure.

DR. DEMAIN MOVED TO AMEND THE MOTION ON BETA-BLOCKERS TO ADD THAT ONE OF EITHER BISOPROLOL, CARVEDILOL OR METOPROLOL SUCCINATE SHOULD BE INCLUDED ON THE PDL. SECONDED BY DR. MACIEJEWSKI. THE MOTION PASSED UNANIMOUSLY.

19. Review Minutes from November 16, 2007

This item was postponed to the next meeting.

20. Final Comments by Chair or Other Members

The committee discussed the testimony provided by the drug company representatives. Dr. Maciejewski suggested changing the time limit, because three minutes was such a short amount of time. Dr. Brodsky suggested following the lead of other states by not taking any testimony from the drug company representatives. The information is not really helpful in the decision making process, because they do not provide unbiased presentations. Dr. Conright agreed that generally the presentations were not useful in making decisions, but occasionally there is useful information presented. She suggested defining the elements that needed to be addressed to be useful to the committee. Dr. Sater said some states only allowed people to speak if there was new information available on their drug. Dr. Maciejewski suggested allowing the representatives four minutes to present new information. Dr. Sater said she would distribute a table of what the other First Health state do for the committee's consideration. She suggested that no change be made during this cycle of meetings, but before the next cycle begins.

The committee continued to discuss the testimonies. Dr. Malter asked if the committee could change the rules or if there were regulations stating that testimony had to be accepted. Mr. Campana said there were no regulations and it was up to the committee to set their procedures by a consensus vote.

Dr. Demain pointed out that the problems with the sound system were very distracting. He felt they needed to invest money in different equipment or fix the equipment. Dr. Conright agreed and noted that several of the telephone conversation could not be heard. Several people on teleconference noted that this meeting was clearer on their end then the previous meetings.

Mr. Campana listed the drugs to be reviewed at the next meeting on April 18, 2008.

The meeting adjourned at 11:30 a.m.