Pharmacy and Therapeutics (P&T) Committee Meeting Record

Date: Friday, April 19, 2013 Time**:** 9:00 a.m. – 3:00 p.m. **Location:** Idaho Medicaid, 3232 Elder Street, Boise, Idaho, Conference Room D

Moderator: Perry Brown, M.D.

Committee Members Present: Perry Brown, M.D.-Chair; Greg Thompson, M.D. ; David Calley, PharmD; Tami Eide, PharmD; Kevin Ellis, PharmD; Mark Turner, M.D.; Troy Geyman, M.D.; Jeffrey Johnson, PA-C, PharmD; Leigh Morse, M.D.; Mark Johnston, RPh

Committee Members Absent: Elaine Ladd, PharmD

Others Present: Paula Townsend, PharmD, Magellan Health Services; Mark England PharmD, Magellan Medicaid Administration; Jane Gennrich, PharmD, Division of Medicaid; Chris Johnson, PharmD, Division of Medicaid; Cody Scrivner, Division of Medicaid; Teresa Martin, Division of Medicaid

AGENDA ITEMS	PRESENTER	OUTCOME/ACTIONS
CALL TO ORDER	Perry Brown, M.D.	Dr. Brown called the meeting to order.
Committee Business		
➢ *Roll Call*	*Perry Brown, M.D.*	Dr. Brown completed the roll call. Dr. Greg Thompson, an Internist with St. Lukes was introduced as a new member.
➢ *Reading of Mission Statement*	*Perry Brown, M.D.*	Dr. Brown read the Mission Statement.
➢ *Approval of Minutes from November 16, 2012 Meeting*	*Perry Brown, M.D.*	The November 16, 2012 meeting minutes were reviewed. The minutes were accepted as proposed.
➢ *DERP Update*	*Tami Eide, Pharm.D.*	Dr. Eide gave an overview of current DERP (Drug Effectiveness Review Project) products in process and asked for Committee input on topics to be developed into review products for the May – December 2013 time period. The Committee indicated that they would like to see a report on Drugs to Treat COPD and the Newer Medications for Diabetes.

➢ *Psychotropics in Foster Children Update*	*Tami Eide, Pharm.D*	Dr. Eide gave an update on the use of psychotropic medications in foster children. Dr. Eide reviewed the list of red flags and Idaho Medicaid's current progress on review and quality change implementations. She reviewed the study parameters and results for foster children receiving two or more antipsychotics concurrently within the time period of 4/1/2012 through 9/30/2012. There were 49 patients identified with fills for two or more different antipsychotics for 60 or more days during this time period. The highest utilized drug combination in patients meeting the red flag threshold was for the combination of aripiprazole and risperidone with the second most common combination being for aripiprazole and olanzapine and risperidone. The DUR Board felt that a pharmacy edit should be in place for two or more antipsychotics for more than 60 days. The most recent study for utilization of ADHD drugs in Foster Children was also reviewed. This study reviewed claims of any foster child receiving an ADHD drug between 11/1/2012 and 1/31/2013. After eliminating 187 children receiving less than two months of any drug, 572 children were evaluated. The study evaluated dosage issues, treatment patterns and duplicate therapy. Potential inappropriate use was identified in only 20 patients. The committee discussed the results and felt that there were no policy concerns, but felt that this was an opportunity to do some targeted education with medical providers of outlier patients.
Public Comment Period	Perry Brown, M.D. Cody Scrivner	**<u>Public Comment Period</u>** Six (6) people signed up to speak during the public comment period. Public testimony was received from the following speaker's:

Speaker	Representing	Agent	Class
Dr. Peter Roan	Self	apixaban	Anticoagulants
Dr. Chris Hammerle	Self	Incivek/Victrelis	Hepatitis C Agents
Bruce Jenkins	Self	Growth Hormone	Growth Hormone
Leigh Platte	Astellas	Vesicare & Myrbetriq	Bladder Relaxant Preparations
Sue Heineman	Pfizer	Toviaz	Bladder Relaxant Preparations
Janine Fournier	Novo Nordisk	Victoza	Hypoglycemics, Incretin Mimetics/Enhancers

➢ *DUR Study on Testosterone Injectable*	Chris Johnson, PharmD	**DUR Board Updates –Testosterone Injectable** Dr. Johnson provided an overview of a drug utilization review on injectable testosterone presented at the April 18, 2013 DUR Board Meeting. Currently the topical formulation of testosterone requires a prior authorization, but injectable testosterone (testosterone cypionate and testosterone ananthate) does not require prior authorization. This study evaluated if testosterone injections were being prescribed appropriately and if there were duplicative treatments between the outpatient pharmacy benefit and medical benefit. Pharmacy 2012 data included a total of 152 participants with 532 claims, whereas medical claims data included 104 participants with 533 claims. There were 15 participants that had both pharmacy and medical claims, with 5 participants having pharmacy and medical claims on the same dates. Dr. Johnson reviewed patient diagnosis for pharmacy claims and medical claims. The study showed that 15.75% of pharmacy claims were for patients without a documented diagnosis or for an unapproved diagnosis. On the medical side, 7.65 % of claims were for participants without a documented diagnosis or for an unapproved diagnosis. The DUR concluded that prior authorization of injectable testosterone for therapeutic diagnosis may be necessary to assure appropriate use and maintain consistency for all dosage forms and across the two programs.
Drug Class Reviews and Committee Recommendations		**Drug Class Reviews and Committee Recommendations**
➢ Newer Oral Anticoagulant Drugs	Shelly Selph, MD Investigator, PNW Evidence-based Practice Center	**Newer Oral Anticoagulant Drugs** The DERP summary review of newer oral anticoagulant drugs was presented by Dr. Shelly Selph. Populations included in this review were patients undergoing orthopedic surgery, patients with non-valvular atrial fibrillation and patients who were medically ill. Drugs included were apixaban (Eliquis), rivaroxaban (Xarelto), edoxaban (Lixiana) –not currently available in U.S. and dabigatran (Pradaxa). Comparators included the newer oral anticoagulants compared with each other and to warfarin, unfractionated heparin or low molecular weight heparins. The review found that the evidence for prevention of venous thromboembolic events in medically ill patients was insufficient. Evidence for treatment in medical patients with venous thromboembolic events is limited. In patients undergoing orthopedic surgery, apixaban, rivaroxaban and dabigatran did not differ in preventing systematic venous thromboembolic events. There was better efficacy with dabigatran compared with enoxaparin on some outcomes, but dabigatran was associated with a greater incidence of harms. For non-valvular atrial fibrillation, all drugs when compared to warfarin had tradeoffs between improved effectiveness and increased incidence of bleeding. Lack of an antidote in the case of serious bleeding or overdose is a major concern with the newer oral

		anticoagulant drugs.
➢ Anticoagulants II	Paula Townsend, PharmD Magellan Health Services	**<u>Anticoagulants II</u>** Dr. Townsend reviewed clinical studies of the new drug apixaban (Eliquis), an oral direct factor Xa inhibitor. The FDA approved indication for apixaban is to reduce the risk of stroke and systemic embolism in patients with non-valvular atrial fibrillation. She also reviewed the 2012 AHA (American Heart Association) /ASA (American Stroke Association) guidelines in which warfarin, dabigatran, rivaroxaban and apixaban are all indicated for the prevention of first and recurrent stroke in patients with non-valvular atrial fibrillation. Dr. Townsend then reviewed the indication update and clinical studies supporting rivaroxaban (Xarelto) for acute treatment of DVT and pulmonary embolism, and to reduce the risk of recurrence of DVT and PE after initial treatment. She also reported on an update of the clinical trial section of Pradaxa showing dabigatran superior to warfarin in reducing ischemic and hemorrhagic stroke in patients with atrial fibrillation in the RE-Ly trail. In addition the FDA's sentinel initiative review of Pradaxa found major bleeding for new user of Pradaxa was not higher than for new users of warfarin. Dr. Townsend reviewed actual utilization of the newer oral agents, as well as warfarin and the low molecular weight heparin class. **Committee Recommendations** The committee reviewed the injectable agents and concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents and that preferred status should be based on cost-effectiveness. The committee then reviewed the oral anticoagulants and concluded that apixabin (Eliquis) had some advantages and recommended placing it on the preferred list and requiring a prior authorization for rivaroxaban (Xarelto).
➢ Platelet Aggregation Inhibitors	Paula Townsend, PharmD	**<u>Platelet Aggregation Inhibitors</u>** Dr. Townsend gave an update from the 2013 ACCF/AHA (American College of Cardiology Foundation and American Heart Association) Guideline for the Management of ST-Elevation Myocardial Infarction. She reviewed the Class 1 recommendations that relate to antiplatelet drugs. She also reviewed the TRIOLOGYACS clinical trial which was for prasugrel versus clopidogrel which showed no significant difference in outcomes. **Committee Recommendations**

		The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents and that preferred status should be based on cost-effectiveness.
➢ Angiotensin Modulators/Angiotensin Modulator Combinations	Paula Townsend, PharmD	**Angiotensin Modulators/Angiotensin Modulator Combinations** Dr. Townsend provided a review of the guideline update from the 2013 ADA (American Diabetes Association) Standard of Medical Care. The pharmacological therapy for patients with diabetes and hypertension should be a regimen that includes either an ACEI or ARB. If one class is not tolerated the other should be substituted. Two or more antihypertensive drugs are generally required to control blood pressure. She reported that the FDA has required that a fetal toxicity boxed warning be added to labeling of all ACE inhibitors, ARBS and aliskiren-containing products. These agents are all now classified as Pregnancy Category D. She also reviewed the contraindication of aliskirin in patients with diabetes and the product discontinuation of Valturna (valsartan and aliskerin) by Novartis in April of 2012. She announced new generics on the market candesartan /HCTZ (for Atacand HCT), eprosartan (for Teveten), irbesartan/HCTZ (for Avalide) and valsartan/HCTZ (for Diovan HCT). **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents and that preferred status should be based on cost-effectiveness.
➢ Beta Blockers	Paula Townsend, PharmD	**Beta Blockers** Dr. Townsend announced that there was no new significant clinical information for this class. **Committee Recommendations** The committee concluded that there were no evidence-based differences to support preferring any agent over another in this class.
➢ Calcium Channel Blockers	Paula Townsend, PharmD	**Calcium Channel Blockers** Dr. Townsend announced that there was no new significant clinical information for this class. **Committee Recommendations** The committee concluded that there were no evidence-based differences to support preferring any agent over another in this class.

➢ Lipotropics, Other	Paula Townsend, PharmD	**<u>Lipotropics, Other</u>** Dr. Townsend provided a review of one new product, icosapent ethyl (Vascepa). This is an ethyl ester of eicosapentaenoic acid derived from fish oil. It is FDA approved for adults with severe hypertriglyceridemia. The two placebo-controlled trials that she reviewed showed no significant change in LDL which differs from the EPA/DHA combinations which show an increase in LDL The effects on cardiovascular mortality and morbidity in patients with severe hypertriglyceridemia have not been established with Vascepa. **Committee Recommendations** The committee reviewed the Bile Acid Sequestrants, Fibric Acid Derivatives, Niacin, Omega-3, and Cholesterol Absorption Inhibitor categories separately. The committee did not feel that there was any efficacy or safety evidence to support change to existing agents in any of the above categories. For icosapent ethyl (Vescepa) the committee recommended that based on the lack of outcome data that it should be non-preferred with a required prior authorization. They recommended that Zetia (ezetimibe) continue to be non-preferred.
➢ Lipotropics, Statins	Paula Townsend, PharmD	**<u>Lipotropics, Statins</u>** Dr. Townsend reviewed information from a retrospective, case controlled observational analysis of administrative databases in Canada, UK and US with over 2 million patients newly treated with statins. The study concluded that patients without pre-existing kidney disease on high potency statins were 34% more likely to be hospitalized with acute kidney injury within 120 days of starting therapy than patients on lower potency statins. **Committee Recommendations** The committee felt that there were differences among the agents. They felt rovsuvastatin had some advantages when a high potency agent was needed or there were potential drug interactions. They felt other agents preferred status should be considered based on cost effectiveness. They recommended that Simcor be non-preferred. The committee also recommended keeping the current restrictions on simvastatin doses > 40 mg/day limiting use to current patients who are tolerating the high dose.
➢ Hypoglycemics, Insulin	Paula Townsend, PharmD	**<u>Hypoglycemics, Insulin</u>** Dr. Townsend reviewed the new AAP (American Academy of Pediatrics) guidelines

		"Management of Newly Diagnosed Type 2 Diabetes Mellitus (T2DM) in Children & Adolescents". She reviewed the FDA action which includes a warning of fluid retention and heart failure with TZDs (thiazolidinediones) in combination with insulin. She announced that insulin lispro (Humalog) is now approved for intravenous administration and that insulin detemir (Levemir) now has an expanded indication for ages 2-5 years with Type 1 Diabetes. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents and that preferred status should be based on cost-effectiveness. They specifically recommended switching levemir from non-preferred to preferred status if not cost prohibitive.
➢ Hypoglycemics, Incretin Mimetics/Enhancers	Paula Townsend, PharmD	**Hypoglycemics, Incretin Mimetics/Enhancers** Dr. Townsend announced FDA approval of a new DDP-4 enzyme inhibitor, alogliptin (Nesina) which It is also available as alogliptin plus metformin (Kazano) and alogliptin plus pioglitazone (Oseni). She reviewed the clinical trials of alogliptin and related combinations. She also reviewed the ADA 2013 Standards of Medical Care in Diabetes and the 2012 ADA/European Association for the Study of Diabetes Consensus Statement. She discussed the FDA Alert published in March of 2013 which stated that patients with Type 2 Diabetes treated with DPP-4 inhibitors or GLP-1 agonists may be at increased risk for pancreatitis and pancreatic cancer. Dr. Townsend then discussed the study of exanatide ER (Bydureon) vs liraglutide (Victoza) which showed a greater decrease in baseline A1c with liraglutide, but a higher incidence of some adverse effects. **Committee Recommendations** The committee reviewed the DPP-4 Inhibitors and Combinations group first and concluded that there were no evidence based differences to support preferring any agent over another in this group. The committee then discussed the incretin mimetics. The committee felt that there were therapeutic reasons to recommend Victoza over Byetta.
➢ Hypoglycemics, TZD	Paula Townsend, PharmD	**Hypoglycemics, TZD** Dr. Townsend announced two new generics: pioglitazone (for Actos) and pioglitazone plus metformin (for Actoplus Met). There was no new significant clinical data to present.

		Committee Recommendations The committee concluded that there were no evidence based differences to support preferring any agent over another in this class and that preferred status should be based on cost-effectiveness.
➢ Proton Pump Inhibitors	Paula Townsend, PharmD	**<u>Proton Pump Inhibitors</u>** Dr. Townsend announced that *clostridium difficile* associated with diarrhea was added to warnings and precautions for pantoprazole (Protonix). No new significant clinical information was presented. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents and that preferred status should be based on cost-effectiveness. The committee discussed concern over the high and continuous doses being used and asked that this be sent to the DUR Board for additional research.
➢ PAH Agents, Oral	Paula Townsend, PharmD	**<u>PAH Agents, Oral</u>** Dr. Townsend announced one new generic, sildenafil (for Revatio). There is now a new contraindication for use of ambrisentan (Letairis) in patients with idiopathic pulmonary fibrosis (IPF) with or without pulmonary hypertension. A study of patients with IPF was terminated early due to lack of efficacy and increased risk of disease progression and death. An FDA safety communication and updated warning for sildenafil (Revatio) states that it should not be prescribed to children < 18 years for PAH based on a study which showed children taking high dose of Revatio had a higher risk of death than children taking a low dose. Low doses were not effective in improving exercise ability. The Department indicated that there had been push back from one local pediatric cardiologist on the FDA decision. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents and that preferred status should be based on cost-effectiveness. The committee recommended that we discuss the FDA warning with other pediatric cardiologists and pediatric pulmonologists.

➢ Topical Androgenic Agents	Paula Townsend, PharmD	**Topical Androgenic Agents** Dr. Townsend announced that Andro-Gel 1.62% is now available in dose packets containing 1.25 G and 2.5 G gel. There are no significant FDA actions and no new significant clinical information was presented. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents and that preferred status should be based on cost-effectiveness. The committee also discussed the results of the injectable testosterone DUR and recommended that no prior authorization be placed on the injectable, but that continual surveillance for inappropriate use be done.
➢ BPH Treatments	Paula Townsend, PharmD	**BPH Treatments** Dr. Townsend announced a new generic alfuzosin ER (for Uroxatral). Based on post-marketing reported adverse drug reactions, finasteride (Proscar) labeling has been updated to include male infertility, poor seminal quality, depression, erectile dysfunction and decreased libido that continues after discontinuation. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents and that preferred status should be based on cost-effectiveness.
➢ Bladder Relaxant Preparations	Paula Townsend, PharmD	**Bladder Relaxant Preparations** Dr. Townsend reviewed one new drug in this class, mirabegron (Myrbetriq). It is a Beta-3 adrenergic agonist which activates Beta-3 receptors on the detrusor muscle resulting in increased filling and storage of urine without suppressing the amplitude of bladder contractions during micturition. Dr. Townsend reviewed clinical trials related to this new agent. Dr. Townsend also gave an update from the AHRQ Systematic Review- Nonsurgical Treatments for Urinary Incontinence in Adult Women: Diagnosis and Comparative Effectiveness which was published in April of 2012. In summary, benefits from drugs are small and comparative effectiveness evidence about long-term adherence to and safety of all available treatments is insufficient. She also reviewed the American Urological Association Guidelines from 2012 for Diagnosis and Treatment of Overactive Bladder (Non-Neurogenic) in Adults. Gelnique (oxybutynin topical gel)

		is now available in a metered dose pump. Oxytrol (oxybutynin) patches will be going over the counter for women (but not for men). Sanctura XR is now available generically as trospium ER. **Committee Recommendations** The committee discussed the new drug mirabegron (Myrbetriq) as well as provider letters supporting continuing Toviaz and Vesicare as preferred agents. They concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents including mirabegron and that preferred status should be based on cost-effectiveness.
➢ Bone Resorption Suppression and Related Agents	Paula Townsend, PharmD	**<u>Bone Resorption Suppression and Related Agents</u>** Dr. Townsend reviewed one new product, alendronate (Binosto); an effervescent once weekly alendronate formulation which has the same FDA approved indications as the other alendronate products. It was approved based on demonstrated bioequivalence to oral tablets. She reported on drug availability/marketing issues with alendronate. Fosamax 5, 10, 35 & 40 mg tabs are available generically in the marketplace but Fosamax brand is no longer marketed in these strengths. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents and that preferred status should be based on cost-effectiveness. They asked that the Department review new FDA advisory panel information on safety and effectiveness of salmon calcitonin.
➢ Phosphate Binders	Paula Townsend, PharmD	**<u>Phosphate Binders</u>** Dr. Townsend announced that there is no new significant clinical information in this class. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents and that preferred status should be based on cost-effectiveness.
➢ Growth Hormone	Paula Townsend, PharmD Jane Gennrich, PharmD	**<u>Growth Hormone</u>** Dr. Townsend announced that there is no new significant clinical information in this class She

		explained the utilization slide reflects units of drug rather than number of prescriptions used in comparing other drug classes. Dr. Gennrich then reviewed Idaho Medicaid's current Therapeutic Criteria for Growth Hormone therapy. There have not been any major consensus guidelines published in the last year for growth hormone for either Prader Willi or other disease states. With respect to Prader Willi Syndrome, Dr. Gennrich clarified that the FDA approval for growth hormone for this disease state is for Prader Willi children with growth deficiency and not for Prader Willi patients for their entire lifetime. While growth hormone is currently being studied in Prader Willi patients for indication other than linear height such as improved lipid metabolism, there is not definitive evidence at this point that growth hormone is safe and effective for this indication. Idaho Medicaid will review the information that Mr. Jenkins has provided the Committee. With respect to other state Medicaid programs, not all states require prior authorization for growth hormone and therefore those claims will pay at the pharmacy regardless of diagnosis or age of the patient. In addition, that statement made earlier today that growth hormone helps with the hyperphagia (insatiable hunger) of Prader Will Syndrome is contradicted by the evidence that Prader Willi children on growth hormone during the years that they are growing taller are still insatiably hungry. Dr. Gennrich reviewed the other indications for which Idaho Medicaid will cover growth hormone including growth hormone deficiency that has been proven with a growth hormone stimulation test and Turner Syndrome girls; for these indications also, Idaho Medicaid only authorizes growth hormone while the child is still growing taller. Indications that are not covered by Idaho Medicaid include idiopathic short stature and small for gestational age where there has not been a documented growth hormone deficiency as these requests are considered cosmetic and not medically necessary. **Committee Recommendations** The committee endorsed the current Therapeutic Criteria although this topic will be briefly discussed again at the next meeting in May 2013 after the information provided by Mr. Jenkins has been reviewed by Provider Synergies and Idaho Medicaid. The committee also discussed whether patients currently on a non-preferred growth hormone brand should be grandfathered to continue the same brand of growth hormone and the consensus opinion was that this not necessary as only the device changes and not the actual medication.
➢ Growth Factors	Paula Townsend, PharmD Jane Gennrich, PharmD	**<u>Growth Factors</u>** Ingrelex is the only drug in this class covered by Idaho Medicaid. Dr. Townsend announced that there is no new significant clinical information for this drug. There are currently no Idaho Medicaid participants receiving this medication.

		Dr. Gennrich then reviewed Idaho Medicaid's current Therapeutic Criteria for this medication which is taken directly from the FDA approved indication and labeling for Increlex. Idaho Medicaid receives approximately one request every 1 to 2 years for this drug so it is infrequently prescribed. The indications are children with severe primary IGAF-1 deficiency (insulin-like growth factor) or children with growth hormone gene deletion who have developed neutralizing antibodies to growth hormone. Criteria for initial approval also includes height standard deviation three or more standard deviations below the mean. **Committee Recommendations** The committee endorsed the current Therapeutic Criteria. As there is only one drug in this drug class, it may remain preferred with criteria.
➢ Erythropoiesis Stimulating Proteins	Paula Townsend, PharmD	**<u>Erythropoiesis Stimulating Proteins</u>** Dr. Townsend announced FDA removal of a portion of the REMS for epoetin alfa and darbepoetin alfa. Prescriber and hospital reenrollment every 3 years in the ESA APPRISE Oncology Program has been eliminated. Dr. Townsend briefly reviewed a new drug Omontys (peginesatide) which was approved in March of 2012 for the indication and treatment of anemia due to chronic kidney disease in adult dialysis patients. Omontys (peginesatide) was voluntarily recalled in February of 2013 due to reports of anaphylaxis and patient deaths and until further notice should not be prescribed or used to treat any patient. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents and that preferred status should be based on cost-effectiveness
➢ Hepatitis C Agents	Paula Townsend, PharmD	**<u>Hepatitis C Agents</u>** Dr. Townsend announced that the FDA has required an addition to the telaprevir (Incivek) prescribing information. A boxed warning regarding fatal and non-fatal serious skin reactions, including DRESS, SJS and TEN has been added. Therapy with telaprevir, peginterferon and ribavirin should be discontinued immediately for serious skin reactions. A new indication for boceprevir (Victrelis) includes adding prior null responders to current indications of partial responders and relapsers, making both of the two protease inhibitors indicated for all three groups. She also reviewed a systematic review which examined sustained viral response (SVR) rates and

		long term outcomes from randomized comparative antiviral drug trials in treatment naïve patients. Key results from this review indicated that dual therapy with peginterferon alfa-2b was slightly less effective in obtaining a SVR versus peginterferon alfa-2a and peginterferon alfa-2b showed a lower risk for serious adverse effects but the difference was small. **Committee Recommendations** The committee recommended that both protease inhibitors (Incivek and Victrelis) be preferred. The committee also recommended doing a DUR Study evaluating whether these medications are being used appropriately.
➢ Pancreatic Enzymes	Paula Townsend, PharmD	**Pancreatic Enzymes** Dr. Townsend announced that Pertzye, Viokace and Ultresa (all previously marketed formulations in this class) are now FDA approved. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents and that preferred status should be based on cost-effectiveness
Other Committee Business	Tami Eide, PharmD	**Other Committee Business** Dr. Eide announced that the next P&T Committee meeting is scheduled for May 10th, 2013. There was no other committee business. The meeting adjourned at 3:00 p.m.

Pharmacy and Therapeutics Committee
Public Comment
April 19, 2013

Peter Roan, MD
My name is Peter Roan and I'm a cardiologist in Nampa. I'm actually an employee of Saint Alphonsus and I'm just representing myself. I'm not receiving any compensation for this testimony and I don't have any financial ties to pharmaceutical companies or medical supply companies. I would say that, in my practice, I see a lot of patients with atrial fibrillation and have had for many years. As you know, atrial fibrillation is not a dangerous arrhythmia in and of itself, but it's associated with stroke and systemic embolization, and that's the big fear with this. We've had warfarin for 50 years, but warfarin is an extremely difficult drug to deal with in terms of its interaction with other drugs and food, and all the studies have demonstrated that, even in the best hands, patients are in the therapeutic range with warfarin about 60-65% of the time. So, we definitely need new agents in order to provide anticoagulation for patients that are safe and are effective in preventing stroke and systemic embolization. The strokes that you see with atrial fibrillation tend to be massive strokes. They tend to be disabling and they tend to be fatal about 30% of the time. About half the time, the patients that don't die end up in nursing homes, so it's a very expensive sort of event and very tragic for the families in many situations. So I'm here to speak for apixaban, which is an effective anti-Xa agent that has recently been approved by the FDA, and I think apixaban has several advantages. It does not require monitoring. It's more effective than Coumadin or warfarin in terms of preventing stroke and systemic embolization. It has less major bleeding than warfarin or Coumadin, and it has shown a mortality benefit, which I think is very important in comparison with warfarin. So it's a very effective drug. It seems to have a low rate of major bleeding and it seems to be very safe, and I would encourage its inclusion in the formulary, hopefully on a preferred basis, so that prior authorization wouldn't be necessary. Thank you.

Question
Not being quite as familiar with personal use of this agent, is it reversible?

Peter Roan, MD
No, none of the newer agents are reversible. There is experimental data looking at PCC (prothrombin complex concentrates) and it's thought that that will be effective, but there's really no data at this point.

Question
Have you used all of the newer agents?

Peter Roan, MD
I have.

Question
In comparing them, what would you say?

Peter Roan, MD
Well, as you know, there's no head-to-head comparisons. There probably never will be. I think apixaban I like because it doesn't have the GI problems that you see with Pradaxa, and it doesn't have the GI bleeding problems that Pradaxa has, and when you look at Xarelto, Xarelto was just not inferior to warfarin. It wasn't superior and Apixaban is superior to warfarin in terms of preventing stroke. So I think it has some definite advantages. Thank you.

Christopher Hammerle, MD
My name is Christopher Hammerle. I am a gastroenterologist here in town, practicing at Idaho Gastroenterology and am speaking with you today about hepatitis-C therapy, in particular, telaprevir, a new protease inhibitor that's been available now since 2011. As you all know, Hepatitis C is a very common condition that we see in our communities. It is estimated that 3-5 million Americans are afflicted with Hepatitis C and that's probably an underestimation. We see it on a daily basis; in fact, it seems to be making up a greater percentage of my patient population on a day-to-day basis. The vast majority of Hepatitis C patients are asymptomatic and, unfortunately, they don't come to our attention until they get screened for another medical condition, or executive physical, or donate blood, etc., when it becomes apparent at that time that they have Hepatitis C. It is estimated that maybe 1 in 30 baby boomers are now infected with Hepatitis C and the CDC (Centers for Disease Control)just recently issued some guidelines saying that anyone born between the years 1945 and 1965 should have testing for Hepatitis C at least one time at this point. Treatment for Hepatitis C has been historically somewhat frustrating, especially genotype-1 patients. The cure rates for Hepatitis C historically have been around 30% or so. In 2011, two new drugs hit the market, one boceprevir, the other telaprevir, both protease inhibitors, that markedly improved our success rate for treatment of particularly genotype-1 patients with Hepatitis C. Both have shown efficacy, both have their merits. Personally I think that telaprevir is the superior of the two drugs and is something now that I use in my practice exclusively. I have used both drugs. Both have, like I said, some efficacy, though it seems that telaprevir is slightly superior, and the reason for that is that patient compliance is probably the biggest driving factor, in my opinion, for the successful treatment of patients with chronic Hepatitis C. We need to take patients from day-1 through treatment, and they need to be completely compliant with medications, and telaprevir is a much easier medication to take in terms of dosing schedule, the regimen we've used, and the exposure time that the patients are actually on the drug. Telaprevir they're on for shorter periods of time, the side effect profile, while similar to boceprevir, is probably a little bit lessened, because the patients are, in fact, on the drug for much shorter periods of time; 12 weeks versus sometimes up to 36 weeks with boceprevir. It is a drug that needs to be used in combination with standard interferon and ribavirin, so, of course, patients need to be monitored carefully, but all in all, I've had excellent success with telaprevir and I think it should be included in our armamentarium when we go to treat patients with this disease. Not all patients are the same, not all clinical scenarios are the same, and the two drugs, while similar, are also not the same. They have slightly different side effect profiles, again, slightly different dosing strategies, and I think it's important as a clinician and practitioner to have both at our disposal, and tailored individually for every patient.

Committee
Any questions? Thank you very much. Okay, we're finished with the medical practitioners. We'll go onto private citizens. Bruce Jenkins?

Bruce Jenkins
Hi, I'm Bruce Jenkins. I'm just a normal person here, so I'm not going to have all the great terminology that these doctors will have. We're here to talk a little about Prader-Willi syndrome and the treatment and procedures that have been proved. One in particular, the growth hormone therapy. As you probably know, Prader-Willi syndrome is a rare genetic disorder. It's not very common, in fact there's only about (that we know of) in the Prader-Willi Idaho organization here, about 27 individuals in the state of Idaho. But some of the characteristics of the Prader-Willi syndrome are like, well, when our daughter was born, they called her "floppy baby". They have very low muscle tone. In fact, she could not eat with a bottle or any other nursing methodology, so from day-1, she was fed through a tube for the first year. The best treatment for this, one of the things that they have with Prader-Willi, is an insatiable hunger desire. They cannot turn off their hunger. So, in our home for instance, every single piece, every food option we have is locked up; the refrigerator, pantries, cupboards, because they have a tendency to forage, steal, and do everything they can to get food, and that problem results in obesity and they have other cognitive disorders and things like that, that are very difficult to deal with. One of the best treatments that have been found, and is the standard being used today and approved by the FDA, and the standard in the medical industry right now, is the use of what's called growth hormone. Unfortunately, growth hormone has been categorized as something just to improve the height of an individual and, I think that based on the Idaho's statement here for that approval was medical necessity documentation for growth. Unfortunately, for Prader-Willi individuals, height is not really the issue. What happens when these individuals take the growth hormone, is that it improves their overall ability to ingest their calories, to burn them off. It improves their muscle tone, it improves everything that they have. Now, I had a stack of documents here, studies that I was going to present to you today for your consideration, but being new, again, like I said I wasn't aware that that had to be preapproved, so I feel bad that as you discuss this later in the day, you may be aware of some of these things, but you may not. But I guess, in summary, or in basis here, what growth hormones does is they increase the protein synthesis, increase muscle mass, reduce fat mass, beneficial effects on lipid and metabolism, and alterations in carbohydrates. Prader-Willi individuals inherently have low levels of growth hormone in their bodies inherently. Obviously, that's why they have the situation that they have, and as they go into adulthood as all adults do, they decrease that growth hormone in their bodies, so the studies are showing; actually a very excellent two-year study that was conducted with a placebo effect, was done to show that using growth hormone in Prader-Willi syndrome individuals as adults as well as in children, that as adults, they were extremely effective. Our daughter, well she just left, was diagnosed with that when she was born. She was not able to get growth hormone until she was almost nine years old. In that time, she had very low muscle mass, very low ability to move, it took her a long time to get up to walk and to crawl, and to do all those things. As a consequence, she has a very difficult scoliosis, which they had an operation to put a rod in her back and things like that to help her. What we're appealing to you is to consider the use of growth hormones for these children. It's the only thing that's really effective to help them. Right now, she's denied because her bone age has reached the point where it's been determined that the growth hormone won't work anymore for her height, but that's not the case because they really need this. To be honest with you, Prader-Willi syndrome is one of the most (I'm sorry) [unintelligible] I did not expect to be emotional at all. Prader-Willi syndrome is probably one of the most cruel syndromes there is, not only for the child, for the individual, but for the caregiver.

We cannot leave her out of our sight, she cannot go to activities with her youth programs or other things and enjoy the treats. She has to stay on the side and not eat those. She is the way she is today. She does not look like a typical Prader-Willi syndrome individual. It is only because of the growth hormone therapy that she has received in the past and because of the absolute vigilant nature that we've had to have, and especially her mother has had to have, in order to protect her from the restrictive diet. What happens is, if she goes off the growth hormone, even though we restrict her diet down to even 800 calories a day, which is almost ridiculous, she will still gain weight, because she doesn't have the metabolism to burn it. So I appreciate this. Her doctor, Dr. Boston, who is in Oregon, an endocrinologist who is one of the best and worked very much with Prader-Willi syndrome individuals, has asked and recommended continued use of growth hormone for her particularly, and I do not feel like.... in a way, yeah, there's only 27 in the State, so we might think that's not a big population to consider, but I want you to realize that those are still individuals and they have parents and they have siblings that they have to deal with, so I would submit that those 27 would not be over burdensome for the state to continue to allow that for these individuals. Thank you.

Committee Question
I just have two questions and a comment. This is important and may be, I think there's data that I think we should look at. I'm not familiar with the data, so I think giving it a serious look see is important. As you say, it's 27 that we know of, individuals who are affected, but do you know, does Oregon approve this for their population? Their Medicaid equivalent population?

Bruce Jenkins
I know Utah does.

Mrs. Jenkins
Oregon does not and Dr. Boston has mentioned quite adamantly about this.

Committee
Okay, so some states do.

Bruce Jenkins
Yeah, there are quite a few. Utah does. There's a number. I didn't have a chance to look up how many there were, but it is an approved standard from the FDA for this to be used for Prader-Willi individuals and it's a typical standard. What happens is, is that from childhood to adulthood, to the point where their growth plates have not been reached it's approved. What happens is, typically they say "Well, you're finished growing, so you don't need it anymore".

Committee
Do you know at all your sense of the data and what's published, is there any data or studies done to show what happens when they're taken off, I mean you tell us, but has that been looked at? Any longer term data? So they get it until the growth plates are closed, and then have people been

taken off and then followed for more than, uh...

Bruce Jenkins
Yes, yes. There was a two-year study done that was shown here at a scientific conference, it was actually published over in Taiwan. There is a lady here, a PhD, Barbara Whitman, that has done an extensive evaluation of adults and what happens when they're taken off. What happens is, it just, basically they start to go back; obesity, especially in the middle section of their bodies, they can't assimilate the calories so the obesity, the bone mass, and the muscle. Also, mentally is affected. They have to be careful because the irony is that our daughter understands everything that's going on, so she feels bad, but she can't do anything about it. We have noticed that since she's being been weaned off this, is that her speech is starting to slur a lot more, and she can't think well.

Committee
So I was just in there looking at our preferred drug list and prior authorization criteria and for Prader-Willi and a couple of the others, Turner Syndrome, HIV plus cachexia, are approved, and what I'm worried about is that we're getting caught up, You're getting caught up in the situation where the criteria that are used are for growth hormone deficiency and short stature, as opposed to uh, you know, the syndrome-specific situation, so this is something that we will discuss. I can assume, if I recall, that yes, there is a meeting for this afternoon, and we'll take a look at the prior authorization form and make sure that we are appropriately addressing this. I guess my question to you is, she was approved previously under the criteria for Prader-Willi, but then lost approval once bones matured? Is that correct?

Jenkins Family
Yes.

Committee
I will take those articles if you want and we will look at those.

Bruce Jenkins
Thank you, thank you very much.

Committee
Thank you. Okay, that finished private citizen commentary. Next up is the representatives from the drug industry. Leigh Platte?

Leigh Platte
Good morning, I'm Leigh Platte. I'm from Astellas Pharmaceutical. I have a Bachelor of Science and, let's see, you're looking for.... nope, nothing else. I'm here to talk about Vesicare and Myrbetriq, which do you prefer first. Makes no difference? Okay. Vesicare (solifenacin) I'll start with. The data we're presenting today is from the Comparative Effectiveness Report prepared for the Agency of Healthcare Research &

Quality. The AHRQ at the Minnesota evidence-based practice center reviewed nonsurgical difference of urinary incontinence in adult women. Continence was achieved in one woman with urgency for every eight women treated with fesoterodine, twelve with tolterodine, nine with oxybutynin, nine with solfenacin, and nine with trospium. Compared to placebo, all drugs, except darifenacin and tolterodine led to more treatment discontinuation due to adverse events. Discontinuation due to adverse effects occurred more often with fesoterodine or oxybutynin than with tolterodine. The number needed to treat for one discontinuation was the highest with solifenacin; number needed to treat was 78, and the lowest with the oxybutynin; number needed to treat was 16. The absolute rates of adverse effects leading to a treatment discontinuation were the highest with oxybutynin and were comparable between other drugs. The most common adverse effect was the highest with oxybutynin. Among other adverse effects were constipation and blurred vision, which were the most common. We request that Vesicare be maintained on the preferred drug list.

The second drug is Myrbetriq. It's a newer compound. Mirabegron is the generic name, and we'd like to present the 12-month data that was published by Dr. Christopher Chapel. It was a 52-week safety study in 2,444 patients randomized to mirabegron or active-control tolterodine. Myrbetriq 50 mg improved key overactive bladder symptoms from first measured time point for four weeks, and efficacy was maintained throughout the 12-month treatment period. Serious adverse events reported by at least two patients and exceeding the active control included cerebrovascular accident (0.4%) and osteoarthritis (0.2%). Serious adverse events of neoplasm reported in 0.1%, 1.3% and 0.5% of patients with the Myrbetriq 50 mg or 100 mg for active control once daily respectively. The most common treatment emergent adverse events reported were hypertension (9.2% versus 9.6%), UTI (5.9% versus 6.4%) and dry mouth (2.8% versus 8.6%). That's in Myrbetriq 50 mg and active control respectively. [Unintelligible] Thank you very much, are there any questions? Thank you, I appreciate the time.

Sue Heineman

Hi, I'm Sue Heineman. I'm with Pfizer as an outcome specialist. I have a PharmD degree and I'm board certified in pharmacotherapy. I am representing Pfizer, and I'm here to respectfully request that fesoterodine remain a preferred agent for the bladder relaxant class. The point that I want to discuss is an article that was not included within the Provider Synergies" review. We did two head-to-head trials with fesoterodine versus tolterodine. These trials were designed because of our registration trials, so the registration trial is included within the Provider Synergies" review, that's the Chapel article, and in Europe, you've got to have an active comparator, so tolterodine which was, essentially the market leader, was the active comparator, and so the post hoc analysis showed that there were some interesting results, but post hoc analyses are hypothesis generating and, therefore, we designed two head-to-head trials. The first one is provided within the Provider Synergies" review, that's the Herschom article, that was the first superiority trial. The second superiority trial, which was not included within the review was by Kaplan, and this was a multi-centered, head-to-head, fesoterodine (Toviaz) versus tolterodine. It was evaluated at the maximum doses of both of these agents. The primary endpoint was achieved; the change in mean number of urge urinary incontinence episodes, so that was superior with fesoterodine, as well as the secondary endpoints showing significantly greater efficacy in reducing urgency and frequency in episodes. There was also a health related quality of life that was included in the first head-to-head trial, the Herschom article. These were post hoc analyses, so again, you can't really make comparisons, but we had time to be able to include them as pre-specified endpoints within the second head-to-head within the Kaplan, and those were also seen statistically significant with the health related quality of life. Your utilization data: the fesoterodine is the third most utilized agent.

It's the second most utilized branded agent. Within the utilization, there are about half the patients on 4 mg of fesoterodine and about half on the 8 mg of fesoterodine, so there are patients who are needing the higher dose. So just in conclusion, I just wanted to make sure you had the data on both of these head-to-head trials. They are superiority. The largest trials we've attempted to evaluate this. Again, I respectfully request that it remain as a preferred agent. Thank you.

Committee
Who funded the trials? The superiority trials?

Sue Heineman
They were funded by Pfizer, right. So the first one was the phase-3 registration trial, and then based on the post hoc analysis, we funded two head-to-head to see, "was this really what we saw in the post hoc analysis with that phase-3 trial?", you know, the problem is that sometimes with the tolterodine, patients need the higher dose, but there isn't a higher dose, and the pharmacokinetics of the fesoterodine makes it more predictable that they will have a response and, so, we just wanted to confirm that with the two trials.

Committee
Alright, Janine Fournier?

Janine Fournier
Hi, I'm Janine Fournier and I am a pharmacist, PharmD, and I am an integrated health system medical science liaison for Novo Nordisk. So my focus today is to provide a quick overview of Victoza, as well as to share with you additional information that wasn't covered on the Provider Synergies" monograph. So first of all, Victoza is a GLP-1 receptor agonist, indicated as an adjunct to diet and exercise to improve glycemic control in adult patients with type-2 diabetes. It is not to be used in patients with a personal or family history of medullary thyroid carcinoma or in patients with multiple endocrine neoplasia syndrome type-2. Victoza should not be used in patients with type-1 diabetes. The most common adverse reaction for the Victoza are headache, nausea, and diarrhea. While there are no conclusive data establishing the risk of pancreatitis with Victoza treatment, Victoza has not been studied in patients with a history of pancreatitis. So other anti-direct therapies should be considered in patients with a history of pancreatitis. There is limited experience with Victoza in patients with renal impairment and in this population, Victoza should be used with caution, though no [unintelligible] should be recommended. So one of the things that I just wanted to give a quick overview first on that, so on the, what I wanted to do was to include on a trial that was published last year that showed that patients who were, it was an extension trial that we had that was 52 weeks and we published now the two-week data that showed that patients who were on sitagliptin for one year and then randomized, so it's a one-year, looking at sitagliptin and Victoza head-to-head, and then they were randomized in extension for an additional 26 weeks. In this particular study, the patients who were on sitagliptin were then randomized to Victoza, and it showed that it achieved additional reductions in glycemic control and weight. Lastly, there was a two-year study evaluating the long-term efficacy and safety comparison of liraglutide and glimepiride all in combination with metformin that demonstrated that Victoza sustained similar reductions in glycemic control, compared to glimepiride and reductions in body weight were reported with Victoza compared to weight gain found with glimepiride. Nausea was

the most common adverse event, but that declined over time. The last point that I want to make is, in addition to our package insert, which was not included as part of the highlighted study with the proprietary monograph, it included that we looked at assessing the addition of basal insulin to a regimen of Victoza and metformin in patients with type-2, which resulted in significant reduction in A1c and fasting plasma glucose. This led to a new indication for the use of Victoza with basal insulin. So that is, I wanted to highlight that, give a quick overview and then highlight the additional data. Any questions?

Committee
When you say "a significant", can you put that into number percentage, or?

Janine Fournier
Yeah, so basically when you look at, with our two-year data, with the long-term that looked at liraglutide and glimepiride, this was a non-inferiority study, it sustained its results, it appeared comparable, so liraglutide 1.2 and 1.8 it was 0.6% and glimepiride it was 0.5% in terms of A1c reduction. Now in that extension of additional patients who were on sitagliptin for one year and then they were switched to liraglutide for a 26 weeks? They were switched to 1.2 mg. The difference was 0.2% of A1c, but it was statistically significant, and with the 1.8 mg of liraglutide, it was 0.5% A1c reduction. .

Committee
Any other questions? No? Thank you.

Janine Fournier
Thank you.