Pharmacy and Therapeutics (P&T) Committee Meeting Record

Date: Friday, April 24, 2015

Time: 9:00 a.m. – 3:30 p.m. **Location:** Idaho Medicaid, 3232 Elder Street, Boise, Idaho, Conference Rooms D

Moderator: Perry Brown, M.D.

Committee Members Present: Perry Brown, MD-Chair; Tami Eide, PharmD; David Calley, PharmD; Kevin Ellis, PharmD; Mark Turner, M.D.; Troy Geyman, MD; Jeffrey Johnson, PA-C, PharmD; Stephen Carlson, PharmD; Chris Streeter, MD; Berk Fraser, RPh; Leigh Morse, M.D.; Brian K. Crownover, M.D.

Committee Members Absent: none

Others Present: Sarah Martinez, PharmD, Magellan Health Services; Mark England, PharmD, Magellan Medicaid Administration; Chris Johnson, PharmD, Division of Medicaid; Jane Gennrich, PharmD., Division of Medicaid; Tammy Haugland, Division of Medicaid; Rachel Strutton, Division of Medicaid

AGENDA ITEMS	PRESENTER	OUTCOME/ACTIONS
CALL TO ORDER	*Perry Brown, MD*	*Dr. Brown called the meeting to order.*
Committee Business		
➢ *Roll Call*	*Perry Brown, MD*	Dr. Brown completed the roll call and welcomed the P&T Committee members.
➢ *Reading of Confidentiality and Mission Statements*	*Perry Brown, MD*	Dr. Brown read the Confidentiality and Mission Statements.
➢ *Approval of Minutes from November 14, 2014 Meeting*	*Perry Brown, MD*	The November 14, 2014 meeting minutes were reviewed. The minutes were approved as proposed. Dr. Eide provided a follow-up on Nurse Practitioner prescribing of psychotropic drugs for foster children. Of the 97 individual nurse practitioners, 30 were solo practitioners responsible for 37%

		of nurse practitioner prescribed claims.
➢ *DERP Update*	*Tami Eide, PharmD*	**DERP Update** Dr. Eide provided an update on drug class reviews currently in progress by the Drug Effectiveness Review Project (DERP): • Direct Acting Antiviral Drugs for Hepatitis C Update • PCSK9 inhibitors • ADHD Drugs - update • Long Acting Opioids - update • Long Acting Insulin Dr. Eide also reported on the current topics up for consideration for the next evidence reviews. • Oral anticoagulants – update • Biosimilars/Biobetters/Copy Cat Drugs • Multiple Sclerosis Drugs – update • Targeted Immune Modulators –update

➢ *Update on Idaho Medicaid Hepatitis C Antiviral Utilization*	*Christopher Johnson, PharmD*	**Update on Idaho Medicaid Hepatitis C Antiviral Utilization**
		Dr. Johnson provided an update on prior authorization requests for Hepatitis-C agents for the time period 1/1/2014 to 3/31/2015. He reported on the outcomes of the requests, the approved agent/genotypes, as well as approval and denial rates. The Department has received 111 requests during this time period with the following outcomes.
		• 41(37%) approved
		• 51 (46%) denied
		  o 46 did not meet fibrosis score criteria
		  o 4 met fibrosis score criteria, but had documented active substance/alcohol abuse
		• 19 (17%) incomplete information. Returned to the prescriber, but no re-request received.
		
		The committee inquired on standardized criteria related to toxicology screening and how long a person must remain drug and alcohol free to be able to receive Hepatitis C treatment. Dr. Johnson reported that there were no identified standard requirements, but the majority of states we have been in contact with require six months.

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<td>Public Comment Period</td>
<td>Perry Brown, MD
Tammy Haugland</td>
<td><u>Public Comment Period</u>
Two people signed up to speak during the public comment period. Two manufacturer representatives were pre-approved to provide testimony. Public testimony was received from the following speaker's:

<table>
<tr><th>Speaker</th><th>Representing</th><th>Agent</th><th>Class</th></tr>
<tr><td>Penny Beach, M.D.</td><td>Self</td><td>Harvoni</td><td>Hepatitis C</td></tr>
<tr><td>Daniel Flynn, M.D.</td><td>Self</td><td>Norditropin</td><td>Growth Hormone</td></tr>
<tr><td>Laura Litzenberger, Pharm.D.</td><td>Janssen Scientific Affairs</td><td>Xarelto</td><td>Anticoagulants</td></tr>
<tr><td>Laura Litzenberger, Pharm.D.</td><td>Janssen Scientific Affairs</td><td>Invokana/Invokamet</td><td>Diabetes medications and combinations</td></tr>
<tr><td>Stewart O'Brochta, R.Ph.</td><td>Gilead Sciences</td><td>Harvoni</td><td>Hepatitis C</td></tr>
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<td>➢ Direct-Acting Antiviral Agents for Hepatitis C Infection</td>
<td>Shelly Selph, MD Pacific Northwest Evidence-based Practice Center</td>
<td><u>Direct-Acting Antiviral Agents for Hepatitis C Infection</u>
Dr. Selph presented the systematic evidence review for a report regarding the Direct-Acting Antiviral Agents (DAA) for Hepatitis C Infection (HCV). The evidence did not allow either direct or indirect comparisons of oral DAA regimens.

Dr. Selph reported on the major findings.
• In HCV genotype 1, inclusion of ribavirin in oral DAA regimens did not affect SVR but increased harms
• Treatment-naïve genotype 1 patients taking ledipasvir/sofosbuvir for 8 week vs 12 weeks had an increased risk of relapse.
• In treatment-experienced genotype 3 patients, SVR rates were lower with 12 than with 16 weeks treatment with sofosbuvir and ribavirin.
• Stage of disease affected response to both the paritaprevir/ritonavir/ombitasvir/dasabuvir plus ribavirin regimen and ledipasvir/sofosbuvir in treatment experienced patients or those with mixed treatment history. In patients with cirrhosis, shorter treatment durations were associated with lower SVR and/or relapse rates, while in those without cirrhosis duration did not affect benefits.
• There was good correlation between SVR12 and SVR24 in oral and other DAA
• regimens, but no evidence on SVR and any long-term outcome in patients given DAAs.</td>
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		• No differences were seen between subgroups in effect of ribavirin, dose, or treatment duration on SVR.
➢ *Drug Class Review – Hepatitis C Agents*	*Sarah Martinez, PharmD Magellan Health Services*	**Drug Class Review – Hepatitis C Agents** Dr. Martinez reported on two new products: Harvoni (ledipasvir/sofosbuvir) and Viekira Pak (ombitasvir, paritaprevir, ritonavir, dasabuvir). She provided a report on the product indications, contraindications, warnings, common adverse effects, and dosage. She also reported that Olysio is now indicated for combination therapy with Sovaldi. Dr. Martinez provided an overview of the updates to the Joint American Association for Liver Disease and Infectious Disease Society of America recommendations for testing, managing, and treating Hepatitis C. They state that "initiation of therapy should be prioritized to patients who would experience the most benefit from receiving treatment and patients whose treatment would have the greatest impact in reducing further HCV transmission" She reviewed their recommendations for each genotype.
➢ *Hepatitis C Therapeutic Criteria for Prior Authorization*	*Christopher Johnson, PharmD*	**Hepatitis C Therapeutic Criteria for Prior Authorization** Dr. Johnson reviewed the draft Idaho Medicaid Therapeutic criteria for this drug class. The committee had questions concerning therapeutic criteria for inclusion criteria: Dr. Johnson stated that documentation of compliance with treatment and appointment visits should be documented in the history and physical area of the chart as a discussion with the patient. There were other questions concerning the therapeutic criteria for pregnancy: The criteria will be modified to indicate that pregnancy related criteria is specifically for patients treated with ribavirin. Additional questions were raised on exclusion criteria and prescriber restrictions. Dr. Johnson stated that previous treatment language was changed to specifically address patients with a history of HCV treatment relapse. There were concerns with who is allowed to prescribe due to limited specialties in rural areas. Dr. Johnson noted the prescriber restrictions state the prescriber can be in consultation with a specialist to treat rural patients. Dr. Leigh Morse suggested the use of hair toxicology to test for substance abuse. Dr. Johnson stated he would research this method.

		Hepatitis C Committee Discussion Although this committee does not typically review drug cost as part of the recommendation process, it is well known publically that these are extremely expensive treatment regimens. Newer agents often come to market between P&T meetings. Dr. Eide gave an overview of Medicaid drug cost in general and the rebate process. Dr. Eide stated the Department needs a mechanism to quickly implement supplemental rebate agreements to minimize the cost for high cost drugs. To not do so and wait for the next P&T decision and implementation could have a large impact on the Department budget. Dr. Eide presented a clause to the committee to address the issue of new drugs for this class allowing temporary financial determinations to be made in between meetings (see below). The Department has been very proactive modeling the best drugs for our Idaho specific population specifically around genotype and presence or absence of cirrhosis and would use that as part of the decision process. **Committee Recommendations** The committee concluded that the evidence did show differences in efficacy and effectiveness for different regimens based on genotype. They also felt that there were differences in potential adherence in the different regimens for example all oral regimens vs peg- interferon and/or ribavirin based and 12 week vs 24 week duration. They also identified safety differences between the various regimens and felt Harvoni had a cleaner safety profile than the Viekira Pak especially for drug interactions. The Committee took an official vote (all in favor, none opposed) to give the Department the authority between P&T meetings to make an interim decision on preferred status in the Hepatitis C drug class, based on preliminary evaluation of the comparative evidence, Idaho Medicaid specific participant characteristics and costs considerations. This decision will then be brought to the next scheduled P&T Committee meeting for final approval, adjustment or rejection. If there are any provider concerns with an interim decision then the Department will contact the P&T Committee chairman for guidance. The Department may also contact P&T Committee members by email for advice concerning these decisions.
Drug Class Reviews and Committee Recommendations		**Drug Class Reviews and Committee Recommendations** Committee members were asked to base their recommendations for each drug class on the answers to the following questions: 1. Is there evidence to support clinically significant differences in efficacy or effectiveness between agents? 2. Is there evidence to support clinically significant differences in safety between agents?

		3. Are there any agents that the committee feels strongly must be preferred or non-preferred? 4. Are there any recommendations for changes to PA requirements?
➢ *Angiotensin Modulators/Angiotensin Modulator Combinations*	*Sarah Martinez, PharmD*	**<u>Angiotensin Modulators</u>** Dr. Martinez discussed two) new products: Diovan (valsartan) and Micardis HCT (telmisartan/HCTZ) are now both available generically. Epaned (enalapril/enalaprilat) is now indicated for treatment of symptomatic heart failure. **<u>Angiotensin Modulator Combinations</u>** Dr. Martinez announced that Exforge (amlodipine/valsartan) and Exforge HCT (amlodipine/valsartan/HCTZ) are now available generically. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents in the ACE inhibitor, Angiotensin Receptor Blocker, Direct-renin inhibitor classes or the corresponding combinations.
➢ *Beta Blockers*	*Sarah Martinez, PharmD*	**<u>Beta Blockers</u>** Dr. Martinez reported on two new products. Hemangeol is a liquid preparation of propranolol indicated for proliferating infantile hemangioma. Sotylize (sotalol) is a liquid preparation indicated for treatment of life-threatening ventricular arrhythmias and maintenance of normal sinus rhythm in patients with highly symptomatic atrial fibrillation/flutter. She discussed indications, dosing, product warnings, and common adverse effects for each. She also reported on the drug interactions for Sotylize (sotalol). There is no comparative data available for either of these new products. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. Specifically they felt Hemangeol has no advantages over existing preparations.
➢ *Calcium Channel Blockers*	*Sarah Martinez, PharmD*	**<u>Calcium Channel Blockers</u>** There was no new clinically significant information in this class to discuss.

		Committee Recommendations The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Antihypertensives, Sympatholytic*	*Sarah Martinez, PharmD*	**<u>Antihypertensives, Sympatholytic</u>** There was no new clinically significant information in this class to discuss. It was noted that the majority of use for clonidine and guanfacine is not for the treatment of hypertension, but for ADHD. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *PAH Agents, Oral and Inhaled*	*Sarah Martinez, PharmD*	**<u>PAH Agents, Oral and Inhaled</u>** Dr. Martinez discussed one new product, Orenitram ER (treprostinil) which is indicated for the treatment of pulmonary arterial hypertension, WHO Group 1. She reported contradictions, dosage, warnings and drug interactions. She also reported that Revatio (sildenafil) is now available as a suspension in addition to tablets and that Adcirca (tadalafil) is now contraindicated for concomitant use with a guanylate cyclase stimulator such as riociguat due to potentiation of their hypotensive effects. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Anticoagulants*	*Sarah Martinez, PharmD*	**<u>Anticoagulants</u>** Dr. Martinez reported on one new product, Savaysa (edoxaban) which is indicated to reduce the risk of stroke and embolism in patients with non-valvular atrial fibrillation and for treatment of DVT and PE. In addition to the indications for treatment, she discussed contraindications, dosing and warnings including a black box warning for atrial fibrillation patients with creatinine clearance values greater than 95 mL/min. She reviewed the results of two clinical studies used for approval of Savaysa. She also reported that Eliquis is now indicated for DVT/PE prophylaxis and treatment and discussed highlights of the 2014 updated of the American Academy of Neurology's guidelines for the prevention of stroke in non-valvular atrial fibrillation for Pradaxa and Xarelto.

		Committee Recommendations **Injectable**: The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. **Orals**: The Committee recognized that there were differences in indications and safety between the agents and recommended that several of the newer agents with decreased bleeding risk as compared to warfarin be preferred agents. The committee also concluded that Savaysa offered no advantage to current agents and should be non-preferred. The committee also recommended that the format for class criteria on the PDL document be listed by indication rather than by drug.
➢ *Platelet Aggregation Inhibitors*	*Sarah Martinez, PharmD*	**<u>Platelet Aggregation Inhibitors</u>** Dr. Martinez reported on one new product, Zontivity (vorapaxar). She reported on the indications for treatment, contraindications, dosage and warnings. Zontivity has only been studied is combination with aspirin and/or clopidogrel. She also reported that Brilinta (ticagrelor) can now be crushed and administered in water by swallowing or via nasogastric tube. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness. The committee recommended that Zontivity (vorapaxar) be non-preferred due to safety concerns with bleeding risk and a long half-life. The committee also recommended listing aspirin on the PDL document as Idaho Medicaid now covers this OTC drug.
➢ *Vasodilators, Coronary*	*Sarah Martinez, PharmD*	**<u>Vasodilators, Coronary</u>** There was no new clinically significant information for drugs in this class. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. The committee recommended continuing to have at least on product available in each dosage form (sublingual spray, ointment, patch, oral capsule/tablet) as preferred.
➢ *Lipotropics, Statins*	*Sarah Martinez, PharmD*	**<u>Lipotropics, Statins</u>** Dr. Martinez reviewed the results of the IMPROVE-IT study which compared the efficacy and safety of simvastatin alone with a fixed combination of simvastatin with ezetimibe in secondary prevention. There was a significant reduction in cardiovascular death, myocardial infarction,

		unstable angina, stroke and coronary revascularization with the combination. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. It was recommended to include Vytorin (simvastatin/ezetimibe) as a preferred agent if cost effective.
➢ *Lipotropics, Other*	*Sarah Martinez, PharmD*	**Lipotropics, Other** Dr. Martinez announced two new generics, omega-3 fatty acids for Lovaza and fenofibrate for Lipoprofen. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. The committee recommended switching Zetia to preferred status and updating the criteria on the PDL document.
➢ *BPH Treatments*	*Sarah Martinez, PharmD*	**BPH Treatments** There was no new clinically significant information in this class to discuss. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Bladder Relaxant Preparations*	*Sarah Martinez, PharmD*	**Bladder Relaxant Preparations** There was no new clinically significant information in this class to discuss. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Bone Resorption Suppression and Related Agents*	*Sarah Martinez, PharmD*	**Bone Resorption Suppression and Related Agents** Dr. Martinez reported Actonel (risendronate) is now available generically. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness

		or safety between the agents.
➢ *Androgenic Agents*	*Sarah Martinez, PharmD*	**Androgenic Agents** Dr. Martinez reported on one new product: Vogelxo (testosterone). Four topical products are now available generically: Testim, Vogelxo, Fortesta, and Androgel. The committee reviewed the FDA Update regarding its investigation into the risk of stroke, myocardial infarction, and death in men taking FDA-approved testosterone products. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Newer Diabetes Medications and Combinations*	*Cindy Feltner, MD, MPH RIT-UNC Evidence-based Practice Center (via previously recorded audio)*	**Newer Diabetes Medications and Combinations** Dr. Feltner reported on the streamlined updated systematic DERP review on newer diabetes medications and combinations. The report reviewed comparative efficacy, effectiveness and safety within drug classes as well as between drug classes. There were few head-to-head trials within drug classes or between drug classes, translating to low strength of evidence for comparative HBA1c changes, weight changes or harms outcomes. • Exenatide XR was more efficacious for reducing mean HbA1c than exenatide given twice daily, but was also associated with more injection site reactions. • Liragludtide was also more efficacious than exenatide twice daily for reducing mean HbA1c. • Exenatide XR and liraglutide were both more efficacious than sitagliptin. • Metformin at doses > 1500 mg per day was more efficacious than most DPP-4 inhibitors for reducing HBA1c and was associated with greater weight loss. • There was no difference between canagliflozin and sitagliptin for reducing HbA1c, but canagliflozin was associated with higher rates of genital mycotic infections in women. Since most trials represented a selected population that was primarily white, middle-aged (none > 60 years) , obese adults with only moderately elevated baseline hemoglobin A1c it was unclear if the reductions in hemoglobin A1c found in the included trials would be consistent with what is expected in general practice.
➢ *Hypoglycemics, Metformins*	*Sarah Martinez, PharmD*	**Hypoglycemics, Metformins** This is the first time this drug class has been reviewed by the P&T Committee. Dr. Martinez provided a review of the current metformin products and their utilization as well as an overview of metformin pharmacology, indications, warnings and adverse effects. Based on the 2015

		American Diabetes Association Guidelines, she discussed metformin as the recommended initial therapy in the treatment of diabetes. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the different dosage forms of metformin. To encourage the use of metformin as an initial agent, it was suggested that there not be therapeutic prior authorization criteria.
➢ *Hypoglycemics, Incretin Mimetics/Enhancers*	*Sarah Martinez, PharmD*	**<u>Hypoglycemics, Incretin Mimetics/Enhancers</u>** Dr. Martinez provided an overview of three new drugs. Glyxambi (empagliflozin/inaglipitin) is a combination of a SCLT2 inhibitor and a DPP-4 enzyme inhibitor. Tanzeum (albiglutide), and Trulicity (dulaglutide) are both in the incretin mimetic class. She reported on the indications for treatment, contraindications, dosing, adverse effects, drug interactions and warnings for each of these drugs. Dr. Martinez provided an update on the SAVOR TIMI-53 study related to cardiovascular outcomes with saxagliptin. There were no changes to the 2015 American Diabetes Association guidelines from the 2014 guidelines with respect to this drug class. **Committee Recommendations** The committee recommended that at least one weekly incretin mimetic agent be preferred. They recommended that saxagliptin be non-preferred for safety reasons. It was recommended that the DUR Board do a study to encourage best practice and appropriate place in therapy for this class of drugs.
➢ *Hypoglycemics, SGLT2*	*Sarah Martinez, PharmD*	. **<u>Hypoglycemics, SGLT2</u>** Dr. Martinez reported on three new products: Jardiance (empaglifloxin), Invokamet (canagliflozin/metformin), and Xigduo (dapagliflozin/extended release metformin). She reported on the indications for treatment, contradictions, dosage and warnings for each, including clinical trials. The 2015 American Diabetes Association guidelines recommendations have moved this class to a second-line therapy, among most other drug classes, behind metformin. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy and effectiveness between the agents. There was some concerns safety wise with Farxiga and its bladder cancer warning. They recommended that these agents be second line therapy, requiring a trial of metformin and possibly one other agent prior to use.

		It was also suggested that the Department make available an educational table showing the comparison of the different antidiabetic agent's ability to lower HBA1c as sole agents and as add on.
➢ *Hypoglycemics, TZD*	*Sarah Martinez, PharmD*	**Hypoglycemics, TZD** Dr. Martinez reviewed the FDA post-marketing study that showed that there was no statistically significant increase in the incidence of bladder cancer among patients taking pioglitazone. She also reported that the 2015 American Diabetes Association recommendations regarding the TZD class of drugs is largely unchanged from the 2014 guidelines. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness and that pioglitazone remain a preferred agent.
➢ *Hypoglycemics, Insulin*	*Sarah Martinez, PharmD*	**Hypoglycemics, Insulin** Dr. Martinez reported on two new products. Afrezza is a rapid-acting inhaled insulin. It must be used with a concurrent basal, long-acting insulin. Toujeo (insulin glargine) is a new long-acting once daily insulin. She reported on the indications for treatment, contraindications, warnings and dosage for each. The clinical trials surrounding FDA approval of these insulins were reviewed. Dr. Martinez also announced that Levemir FlexPen was discontinued in September of 2014, but Levemir FlexTouch is still available. The 2015 American Diabetes Association recommendations for insulins remain the same as the 2014 recommendations. **Committee Recommendations** The committee felt that the evidence supported lower efficacy and effectiveness for Afrezza and concern over pulmonary adverse effects. They asked the pharmacy unit to initiate a manual prior authorization review of this agent. They felt there were safety concerns with Toujeo as its concentration is 300 units per ml rather than 100 units per ml, which could cause dosing problems. Other than these concerns for the new products, they concluded that there was no evidence of differences in efficacy, effectiveness or safety between the insulin products.
➢ *Growth Hormone Criteria*	*Jane Gennrich, PharmD*	**Growth Hormone Criteria** Dr. Gennrich provided a review of Idaho Medicaid's current therapeutic criteria for growth hormone therapy. The committee recommended maintaining the same criteria.

➢ *Growth Hormone*	*Sarah Martinez, PharmD*	**Growth Hormone** Dr. Martinez announced that Genentech is discontinuing production of the Nutropin AQ line of products. The NuSpin products will remain on the market. Zomacton will be the new brand name for Tev-Tropin (April 2015). **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. The committee recommended that preservative-free Genotropin be a preferred agent for children younger than 2 years old who meet Idaho Medicaid's therapeutic criteria. The committee also recommended that Norditropin remain a preferred agent.
➢ *Colony Stimulating Factors*	*Sarah Martinez, PharmD*	**Colony Stimulating Factors** Dr. Martinez reported that as of April 2015, Neupogen is now indicated to increase survival in short-term exposure to myelosuppressive doses of radiation. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Erythropoiesis Stimulating Proteins*	*Sarah Martinez, PharmD*	**Erythropoiesis Stimulating Proteins** There was no new clinically significant information in this class to discuss. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Phosphate Binders*	*Sarah Martinez, PharmD*	**Phosphate Binders** Dr. Martinez discussed one new product, Auryxia (ferric citrate). Auryxia is indicated for the control of serum phosphorus levels in patients with chronic kidney disease on dialysis. She discussed the dosing, contraindications, and adverse effects and discussed clinical trials related to its use. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. The committee recommended making Auryxia a non-preferred

		agent.
➢ *GI Mobility, Chronic*	*Sarah Martinez, PharmD*	**GI Mobility, Chronic** This new drug class designation includes those drugs previously in the Irritable Bowel Syndrome Class. Dr. Martinez discussed one new product, Movantik (naloxogol). Movantik is indicated for the treatment of opioid-induced constipation in adults with chronic non-cancer pain. She discussed the contraindications, warnings, drug interactions, dosing and adverse effects. There is no comparative data available. She also discussed Relistor (methylnaltrexone) and its use in treatment of opiate-induced constipation in patients with advanced illness, receiving palliative care for which response to laxative therapy has been insufficient. It previously was not included in this drug class. Dr. Martinez also reviewed the 2014 American College of Gastroenterology guidelines on treatment of irritable bowel syndrome and chronic idiopathic constipation which includes Amitiza and Linzess as effective treatment options. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents for their designated indications. They recommended having Lotronex as preferred for irritable bowel syndrome with diarrhea and choosing one opioid induced constipation treatment agent as preferred with criteria.
➢ *Pancreatic Enzymes*	*Sarah Martinez, PharmD*	**Pancreatic Enzymes** There was no new clinically significant information in this class to discuss. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. They recommended having at least two preferred options and to consider allowing patients who have failed a preferred agent and are doing well on a non-preferred agent to be allowed to continue on the non-preferred agent.
➢ *Proton Pump Inhibitors*	*Sarah Martinez, PharmD*	**Proton Pump Inhibitors** Dr. Martinez announced that Nexium 20 mg is now available OTC and is also available generically. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. The committee recommended that Prevacid solutabs be a preferred

		agent for children < 5 years, depending on its cost compared to liquid preparations.
➢ *H. Pylori Treatments*	*Sarah Martinez, PharmD*	**H. Pylori Treatments** There was no new clinically significant information in this class to discuss. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Other Committee Business*	*Tami Eide, PharmD*	**Other Committee Business** The next P&T Committee meeting is scheduled for May 22, 2015. There was no other committee business. The meeting adjourned at 3:15 p.m.

Pharmacy and Therapeutics Committee
Public Comment
April 24, 2015

Penny Beach, MD

Hi, I'm Dr. Penny Beach, I'm a family doctor, I'm a founding member at the Family Medicine Residency of Idaho. I'm the director of FMRI's viral hepatitis clinic here in Boise, and assistant professor of family medicine at the University of Washington School of Medicine. I don't have financial ties to anyone. I've never taken a dime of drug money in my life. In fact, I think in terms of hepatitis-C drugs, I've probably cost the companies more than I've made them, because I think I'm the single largest provider who prescribes medications to uninsured patients, which come free through the drug companies' patient assistance programs. So I've been treating hepatitis-C for the past fourteen years, and I just have a few points to make today about hepatitis-C medications. First, I'm here to advocate for Harvoni remaining as at least one of the preferred treatments of choice for genotype-1 hepatitis-C patients. This is because, in my opinion, Harvoni is much safer and more effective than any of the newer options that have come on to the market in the last few months. I have been treating patients with Harvoni, I think I have about three of those patients that Chris put up on the slide there that are Medicaid patients. It's been extremely well tolerated among my patient population. It causes minimal side effects, and even the most marginal patients have been able to complete treatment. I have one guy who has pretty bad schizophrenia and lives in a group home, who would have never considered doing hepatitis-C treatment before this medication came out, and he is now cured and is quite happy about it.

In addition, it's the cheapest option that does not require the use of ribavirin for at least some genotype-1 patients. In my experience, ribavirin can be a dangerous medication. Not always, usually it's fine, but it can be, which can cause costly complications. This fall, I treated a genotype-2 patient with ribavirin and sofosbuvir. This patient had underlying coronary artery disease, so I first sent him to his cardiologist, who cleared him to go ahead with treatment. Two and a half weeks into treatment, after a sudden drop in his hemoglobin, secondary to his ribavirin, my patient suffered a myocardial infarction. He was hospitalized, underwent a coronary artery bypass graft, and had a very expensive three-week hospital stay. He still has hepatitis-C. In contrast, Harvoni does not have these problems. It does not cause anemia and does not cause problems for patients with heart disease. Ribavirin's other potentially costly and heartbreaking complication is teratogenicity, a complication that Harvoni also does not carry. Harvoni is a one-pill-a-day drug. The other newer option, the Viekira Pak, requires patients to take 4-10 pills per day, depending on genotype and whether or not the patient is cirrhotic. The number of pills in the Viekira Pak decrease patient compliance and, thus, I believe, the treatment's practical effectiveness. Both of these new treatments, Harvoni and Viekira, are definitely superior to any of the interferon-containing regimens for genotype-1 patients, even though they are remarkably more expensive. The pegylated interferon regimens are no longer considered standard care by the American Association for the Study of Liver Diseases, because of the very dangerous side effects and their ineffectiveness compared to the newer regimens. Harvoni and Viekira both have cure rates in the 90s. The old regimens with pegylated interferon, it's in the 70s. I have had patients on pegylated interferon with hospitalizations for sepsis, go into decompensated liver failure, and try to kill themselves; all interferon-related side effects. I also wanted to give a little bit of feedback regarding which Medicaid patients should be allowed access to Harvoni or some of the newer, very costly hepatitis-C treatments. Personally, in my ideal world, I'd love it if we could treat everyone, right? But treatment with Harvoni is expensive, but so is treating an end-stage cirrhotic. A March, 2015 study from the Annals of Internal Medicine showed that Harvoni treatment has a cost effectiveness of $12,825 per quality of life year saved, once you factor in all the money you will save by not treating an end-stage cirrhotic. However, I realize that due to the expense of this medication, my dream of universal treatment may not end up as a reality. In this case, I would recommend you follow the AASLD recommendations, that's the American Association of the Study of Liver Diseases, for whom should receive priority for treatment. The first priority is patients with advanced fibrosis, fibrosis stage 3 or 4, patients with cryoglobulinemia with end organ manifestations, such as vasculitis, patients with proteinuria or kidney disease, and organ transplant recipients. The second priority is for patients with stage 2 prior fibrosis, coinfection with hepatitis-B or HIV, coexisting liver disease, such as fatty liver disease, type-2 diabetes, porphyria cutanea tarda, and possibly debilitating fatigue. I actually have a little problem with that criteria, because I think there are a lot of patients and providers that could claim that all of their patients have debilitating fatigue. There is some evidence that treating patients with even stage 2 fibrosis is reasonably cost effective. In a study that has been accepted, but not yet published in the Journal of Hepatology, treatment with twelve weeks of Harvoni resulted in a cost effectiveness of $37,300 per life year saved, again factoring in the money you would save by not treating an end stage cirrhotic. That's it. Thanks for your time.

Committee
Thank you. Anybody have any questions for Dr. Beach? Thank you.

Penny Beach, MD
Can I give written comments anywhere?

Committee
Yes.

Penny Beach, MD
Thank you.

Committee
Thank you for your experience [inaudible]. We have one other physician who is going to be here a little bit later, so we will move on to non-physician, public testimony. I didn't have anyone sign up, is there anyone from the general public who wanted to testify, and are there any physicians that I missed who wanted to testify?

[NO]

Committee
The first person I'll call up, it looks like she gets to bat twice, is Laura Litzenberger, so maybe we'll have you... what we try and do is limit testimony, and I forgot to mention this, to about three minutes each. If you want to speak about Xarelto first, and then we'll go ahead and give you an additional slot of time for, I'm going to mispronounce this, Invokana/Invokamet, is that correct?

Laura Litzenberger, PharmD
Invokana/Invokamet, yes. Good morning, I'm Laura Litzenberger. I'm a clinical pharmacist with the Health Outcomes Research Group at Janssen Scientific Affairs, and as I was introduced, I'm here to provide additional information on Xarelto, which is a Factor Xa inhibitor. This information on dosage and administration was recently put into the prescribing information after your therapeutic clinical review was written. It's a very simple update. As far as being able to crush tablets, prior in the prescribing information, the information was limited to the 15 mg and 20 mg tablets that could be crushed and put in an NG tube or crushed and put on applesauce. The update is that the 10 mg tablet can now also be crushed and administered on applesauce or put through an NG tube. With that, I can entertain any

questions on Xarelto. Okay, thank you very much.

Second, I'd like to speak on Invokana and Invokamet. Invokana is a sodium glucose transporter type-2 inhibitor. It's indicated for the treatment of type-2 diabetes and this information provides additional data in pharmacology, durability of effect, and use in patients with hepatic impairment. So as far as pharmacodynamics and pharmacology, the difference between canagliflozin and dapagliflozin, another SGLT-2 inhibitor, was compared in a randomized, double-blind, crossover study that was published earlier this year. In this phase-1 study involving 54 healthy subjects, 24-hour urinary glucose excretion was analyzed, and that's the way that these drugs work, is by changing the renal threshold for glucose, so as you change the renal threshold for glucose, people eliminate more glucose through the urine and, as you eliminate more glucose through the urine, then you affect the A1c by lowering it. So, in this randomized study, what was done is that patients were either put on canagliflozin (Invokana) or they were put on dapagliflozin. They were treated for four days and then a mixed meal tolerance test was taken, and then compared the excretion of glucose at that point to baseline excretion of glucose, and then there was a crossover. What they found was that there was a 25% increase in glucose excretion in patients when they took the Invokana regimen compared to the dapagliflozin regimen. The dose that was used was the highest dose that was recommended for both drugs, so 300 mg for Invokana and 10 mg for dapagliflozin, so there appeared to be a difference in the amount of glucose that was excreted. Both of these treatments were well tolerated and there were no adverse events. To assess the durability of the effect of canagliflozin or Invokana, there was a comparison to glimepiride and this comparison was a clinical trial that continued for up to 104 weeks. These were patients with type-2 diabetes, who were on metformin, but needed additional glucose control, so they were either put on canagliflozin 100 mg, 300 mg, or glimepiride, and the glimepiride was titrated to 6 mg or 8 mg. The mean dose in the study was actually 5.6 mg. The baseline A1c in these patients was 7.48. The absolute reduction in baseline for canagliflozin 100 mg was 0.68. For canagliflozin 300 mg it was 0.74, and for glimepiride, it was 0.55. So that was at the 104-week time frame, so you can see that the durability was maintained in the canagliflozin group, and when they did the statistical analysis looking at the rate of rise of the A1c, there was a statistical difference between the canagliflozin groups and the glimepiride groups. As far as adverse events, the major adverse events in the canagliflozin group were mycotic infections, urinary tract infections, and were related to the osmotic diuresis. The major side effect in the glimepiride group was hypoglycemic events. Regarding the use of Invokana in hepatically impaired patients, this is just a change in your information. In your information, it said that dosage adjustments are recommended for patients with moderate hepatic impairment. The actual prescribing information says that mild to moderate impairment receives no dosage administration. Invokana has now been studied in patients with severe hepatic impairment. Finally, in the Invokamet information that you received, it indicated that Invokamet was a capsule, and Invokamet is actually a tablet. Do you have any questions on Invokana or Invokamet that I can answer?

Committee
I actually just wondered if I could ask you a quick question on Xarelto? I just wondered if there was anything in the way of pediatric

approval?

Laura Litzenberger, PharmD
The information is being studied. It's not at the point where I would provide any information right now.

Committee
Thanks. Are there any other questions? Thank you very much. All right, then I have Stewart O'Brochta, did I say that right? To talk to us about Harvoni.

Stuart O'Brochta, RPH
Okay, so let me make sure I cover all the things... So, my name is Stewart O'Brochta, I'm a Medical Scientist with Gilead Sciences, and, of course, I do have a financial tie, because I'm employed by them. I appreciate your time today, and the opportunity to come before you and talk about ledipasvir and sofosbuvir combination which is Harvoni, but specifically around the SIRIUS trial, because you have the rest of the information that's in the DERP review. So, specifically, I'd like to go over the SIRIUS trial, which was recently published in Lancet, and it adds to the prescribing availability of Harvoni in a new way that is also reflected in the ASLD guidance as Dr. Beach mentioned. So the SIRIUS trial was a phase-2 trial that was a randomized, double-blind, placebo-controlled, also double-dummy, so basically patients had a ribavirin double-dummy and the ability to not know what they were they were taking based on that. The two arms of the study were the approved labeled use of Harvoni, which is for 24 weeks of once-a-day Harvoni in compensated cirrhotic patients that are treatment experienced. Then, the other arm was a 12-week arm with ribavirin, but that 12-week arm was a placebo lead-in for 12 weeks, so it actually gave the opportunity to measure Harvoni against placebo for 12 weeks, as far as safety and tolerability, and then to go on to Harvoni with ribavirin for the remaining 12 weeks' of therapy. I'd like to point out about the tolerability of that, is, that we only had one discontinuation in the population of patients that were studied, and it was actually in the placebo arm before the patient got to active drug in the 24-week with placebo and Harvoni and ribavirin. As I already mentioned, the study population was genotype-1, compensated, cirrhotic patients. These patients, in their treatment experience, had also failed not only Peg-Riba, they also failed PI therapy, so they were dual therapies on historic therapies when they were put on, so these were very difficult patients. These patients were also, if you're familiar with the CUPIC trial, which was a French trial of very difficult patients to treat, those patients were also patients that had also failed protease regimens and peg-interferon, but they had very low platelets and albumin, and they were all cirrhotic too, and a third of the patients in this trial were CUPIC patients. To compare to the studies that have already been done for Harvoni, this trial was the sickest population that we currently have a published study on, but it's fairly representative of the population that was studied in the Harvoni trials with the ION trials, which was the registration trial. The other important thing about this study is, the ION-2 trial, which I'm not going to talk about because that is part of your packet, the question is "Was that powered well enough in this population of specifically treatment-

experienced cirrhotics?" because in each arm of that trial, there were very few patients when you divided it out per every arm. In this trial, there were 77 patients in each arm, so it was adequately powered to be able to tell a difference in treatment. So, that's another very important point that it asked. As far as resistance testing, we did deep sequencing at baseline and anybody that actually relapsed, and that's another important point. So, we went down to 1% of the isolates, and it didn't affect SVR. We didn't see any resistance with the S282-T mutation, which is the sofosbuvir-based related mutation. Patients, about 16%, had a ledipasvir mutation, but it didn't predict SVR, so at the end of therapy, it was only a 2% difference if you had a mutation going in. So, that's another very important... and we did that on all of our other trials as well. With that said, no one failed on treatment. So there was no virologic failure in any of the registration trials, as well as SIRIUS. The only failure to a Harvoni regimen is based on relapse, and at relapse, those patients were then deep sequenced to see what their results were. The actual efficacy between the two arms was 96% in the sofosbuvir/ledipasvir/ribavirin 12 weeks versus 97% SVR with the labeled 24-weeks in this very difficult population, so no statistical difference, and only a 1% numerical difference between the two. So, while this is a published study, I want to point out that it's not in our label yet, although it is in the ASLD guidelines...

Committee
Just time-wise.

Stuart O'Brochta, RPH
Okay, I haven't got much left, so in closing, which I should have said to let you know I was almost done, so thank you. While it is not in the label yet, it does offer an opportunity now for patients that are ribavirin eligible, as Dr. Beach pointed out, not all patients are, but the patients that can take 12 weeks of ribavirin, you can shorten the course substantially with equal efficacy. So I would ask that you consider, as Dr. Beach did, giving equal access for providers and patients to be able to choose, and now you have an option that may be more economically sound and equally effective for this regimen. So I appreciate your time and I would be happy to answer any questions about this study that you may have. Again, thank you for your time and your consideration.

Committee
Thank you very much.

Daniel Flynn, MD
I'm Daniel Flynn, an endocrinologist. I work with St. Luke's Children's Endocrinology and I'm a hospital-employed physician there. Our practice is located at 222 N. 2nd Street, Suite 215, in Boise. We were asked to speak on behalf of Norditropin from Novo Nordisk. I'm not being compensated at this session. I have done speaking engagements in the past for Novo Nordisk and have done speaking engagements

for other pharmaceutical companies in the past. We wish to talk about growth hormone therapy and a possible preferred formulary change. The concern for our office is that it's somewhat labor intensive every time that there is a change in the different type of growth hormone used. Growth hormone is something that requires training for the delivery device, each delivery device is a little bit different; some are pens, some are syringes, some are computerized delivery devices. Every time that there is a change in the brand or the form that is used, it requires about a one hour to 90 minutes' training session, that's usually done either in an office or by a home health provider, and is generally covered by insurance. So there's usually some interruption in therapy when that's given, and what is important, is that growth hormone, we have it named "growth hormone", but it's really more of an agent that strengthens the skeleton and is good for bone health than merely cosmetic concerns, such as growth. So it really kind of gets a bad rap with the moniker that's been put upon it. We don't like seeing our kids have interrupted therapy when that occurs while they're waiting for training with the new device. The other concerns about a possible change in preparation is that some of the agents, one of the agents that's being considered, is associated with pain, and it is difficult, especially for our younger children, to tolerate the injections. When there's pain associated with it, obviously compliance goes down, and we've seen that in our clinical providers, both myself and my colleague, Dr. Taylor. Why that matters isn't just because we're losing, you know, a little bit of bone health or a little bit of potential final adult height. It's because we have to carefully monitor the safety of growth hormone through testing blood levels, so we have a very narrow therapeutic range that we're trying to attain and to ensure is present, and if we don't know how much has been delivered reliably, or we can't really ensure that there has been optimal compliance, then it really creates a less than optimal set of data for us to make our clinical recommendations. You open up the possibility of increasing risk of some very adverse, long-term outcomes if we naively or misguidedly increase the dose of growth hormone thinking that there has been better compliance than there has, and that has happened on more than a few occasions over the past few years. So those would be the concerns that we have, is that there is going to probably be delay in treatment if there's a brand change, pain associated with the injections, and then decreased benefit from the intervention because you can't have partial compliance with recombinant growth hormone. You need either a six-day or seven-day dosing schedule, and you need fairly rigid compliance with that. With the preparation that's currently on the formulary with Norditropin, it's an agent that has the smallest and the easiest delivery device. It's the only one that does not have to be refrigerated, and it's one of the many preparations that is not associated with pain at injection site, so when we're talking about split families, the pen traveling from person to person, if the pen is left out of the refrigerator in the middle of the night, we're not losing, you know, potentially several weeks' worth of costly product. Those are the concerns that our office has at Children's Endocrinology about the possible change in the preparation of the growth hormone.

Committee
Thank you. Does anybody have any questions for Dr. Flynn?

Committee Question:

So you mention one that was probably worse for injection site pain. Which one is that?

Daniel Flynn, MD
It's Nutropin. There is the preservative that's used in it that's associated with pain. It's more of an issue in small children. The older children are often able to be bribed out of ... [laughter]. But it is something that is a fairly universal complaint.

Committee
Are there any other questions for Dr. Flynn?

Committee Question
If you wanted a preferred second agent after Norditropin, what would you want?

Daniel Flynn, MD
After Norditropin, I'd look at any of the devices that have a pen delivery, or one of the ones that is frequently used for our younger children or children less than two, is Genotropin. I think that would be a very good option, especially for our younger children, because of the preservative profile that's approved for children less than two years of age, so if I had my way, then we'd use those two as the two options at our disposal.

Committee
Any more questions? Thank you very much.