Pharmacy and Therapeutics (P&T) Committee Meeting Record

Date: Friday, November 14, 2014
Time: 9:00 a.m. – 3:30 p.m. **Location:** Idaho Medicaid, 3232 Elder Street, Boise, Idaho, Conference Room D

Moderator: Perry Brown, MD

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; Steven Carlson, PharmD; Chris Streeter, MD; Berk Fraser, RPh

Committee Members Absent: Leigh Morse, MD; E. Gregory Thompson, MD

Others Present: Sarah Martinez, PharmD, Magellan Health Services; Chris Andrews, PharmD, Magellan Health Services; Mark England PharmD, Magellan Medicaid Administration; Chris Johnson, PharmD, Division of Medicaid; Tammy Haugland, Division of Medicaid; Teresa Martin, 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. New member Christopher Streeter, MD, a child and adolescent psychiatrist was introduced.
➢ *Reading of Confidentiality and Mission Statement*	*Perry Brown, MD*	Dr. Brown read the Confidentiality and Mission Statements.
➢ *Approval of Minutes from October 17, 2014 Meeting*	*Perry Brown, MD*	The October 17, 2014 meeting minutes were reviewed. Dr. Geyman moved to accept the minutes, Dr. Turner seconded and the Motion passed. The minutes were accepted as proposed.
➢ *Update on Psychotropics in Foster Children*	*Tami Eide, PharmD*	**Update on Psychotropics in Foster Children** Dr. Eide discussed the GAO study that looked at use of psychotropic drugs in foster children compared to non-foster children in 2008 and included data from 5 states. Idaho has compared

Idaho's foster and non-foster children use of these drugs to this baseline use in 2008, 2011, 2012 and most recently 2013. Idaho was and continues to be comparatively high to these other states for both foster and non-foster children. Foster children utilization increased between 2008 and 2011 and has remained at that level through 2013. Non-Foster children use has remained flat, but relatively high from 2008 through 2013.

Dr. Eide reviewed the percent of total foster and total non-foster children receiving psychotropics by drug class in 2013 for ADHD drugs, antianxiety, mood stabilizers, antidepressants and atypical antipsychotics.

She provided information on claims and cost for foster children and non-foster children. In 2013, overall foster children received an average of 7.91 psychotropic drug claims compared to 1.62 for non-foster children. Cost per foster child for these drugs was $ 756.28 compared to $ 165.14 for non-foster children.

Dr. Eide also presented data comparing breakdown of foster children and non-foster children by age and gender for ADHD drugs, antianxiety drugs, mood stabilizers, anti-depressants and atypical antipsychotics. Prescriber type by claims volume and regional variation for foster children was presented and reviewed. Since nurse practitioners account for 22% of the psychotropic prescriptions in foster children, the committee asked that nurse practitioners be broken out by practice site to separate independent practitioners from those working under a specialist.

Public Comment Period

Perry Brown, MD
Tammy Haugland

Public Comment Period

One person from the public signed up to speak during the public comment period. Two industry representatives were pre-approved to give testimony. Public testimony was received from the following speakers:

Speaker	Representing	Agent	Class
Kathie Garrett*	NAMI Idaho		All Mental Health
Laura Litzenberger, PharmD	Janssen Scientific Affairs	Invega Sustenna	Antipsychotics
Jill Walker, PharmD	Eisai Medical Affairs	Perampanel	Anticonvulsants

*Due to the bad weather conditions, Kathie Garrett was unable to give her testimony in person. Her comments were faxed in and read into the record.

Drug Class Reviews and Committee Recommendations	*Sarah Martinez, PharmD* *Magellan Health Services*	**Drug Class Reviews and Committee Recommendations** Committee members were asked to answer the following questions in each drug class. 1. Is there evidence to support clinically significant differences in efficacy of 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?
➢ *Antipsychotics*	*Sarah Martinez, PharmD*	**<u>Antipsychotics, Atypical (Second Generation)</u>** Dr. Martinez covered both atypical (2nd generation) and typical (1st generation) antipsychotics in her review. There are two new products in this class. Versacloz (clozapine), which is indicated for the treatment of treatment-resistant schizophrenia and for reducing suicidal behavior in patients with schizophrenia or schizoaffective disorder. Efficacy in treatment-resistant schizophrenia was established in a multicenter, randomized, double-blind, active-controlled study. Because of risk of agranulocytosis, it is available only through a restricted program called the Versacloz Patient Registry. Prescribers, patients and pharmacies must enroll in the program. The second new product is Adasuve (loxapine), an oral inhalation product which is indicated for the acute treatment of agitation associated with schizophrenia or bipolar disorder in adults. Adasuve has a black box warning regarding bronchospasm and increased mortality in elderly patients with dementia related psychosis. Other warnings include the development of neuroleptic malignant syndrome or hypotension/syncope and use in patients with history of seizures. Adusave is available through a restricted program called Adasuve REMS and should be administered in an enrolled healthcare facility that has immediate access on-site to equipment and personnel trained to manage acute bronchospasm. Clinical studies used in drug approval were reviewed. There are no comparative studies. Dr. Martinez also reviewed a new study that compared Invega (palaperidone) Sustenna and haloperidol deconaoate in schizophrenia and schizoaffective disorder patients at risk of relapse and meeting criteria for a long-acting injectable antipsychotic. There was no statistically significant difference in the rate of efficacy failure for paliperidone palmitate compared with haloperidol decanoate. The paliperidone group participants experienced higher rates of weight gain and greater increases in serum prolactin whereas the haloperidol subjects experienced more akathesia. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness

		or safety between the agents. There was a recommendation that the typical and atypical agents be separated out on the PDL document. Under the injectables, it was suggested that long-acting and short-acting (acute treatment) agents be separated out. It was asked that the criteria for approval be listed including: - Continuation of non-preferred agents in stabilized patients - Approval criteria justifying more than one antipsychotic - Indications for long-acting injectables The committee recommended having a continuity of care statement in the PDL.
➢ *Antidepressants, SSRI*	*Sarah Martinez, PharmD*	**<u>Antidepressants, SSRI</u>** Dr. Martinez indicated that there was no significant new clinical data in this drug class. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Antidepressants, Other*	*Sarah Martinez, PharmD*	**<u>Antidepressants, Other</u>** Dr. Martinez announced three new products in this class. This first is Fetzima (levomilnacipran), indicated for the treatment of major depressive disorder and administered once daily. There is a black box warning for suicidal thoughts and behaviors in children, adolescents and young adults. Other warnings include serotonin syndrome, elevated blood pressure and heart rate and abnormal bleeding. The second is Khedezia (desvenlafaxine ER base), indicated for the treatment of major depressive disorder. It is not AB-rated to Pristiq. Khedezia is also available as a generic. Efficacy was established in four 8-week, randomized, double-blind, placebo-controlled studies in adult outpatients with major depressive disorder. The last new product is Brintellix (vortioxetine), indicated for the treatment of major depressive disorder with a black box warning regarding suicidal thoughts and behaviors in children, adolescents and young adults taking antidepressants. The targeted dose is 20 mg/day. A new generic now available in this class is another desvenlafaxine ER generic, a fumarate salt. This product is not AB-related to Pristiq.

➢ *Stimulants and Related Agents* ➢ *Sedative Hypnotics*	*Sarah Martinez, PharmD* *Sarah Martinez, PharmD*	No comparative trials were done with any of these agents. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. The Department was asked to consider making venlafaxine immediate release a preferred agent. Dr. Geyman recommended having duloxetine as preferred as it is useful for patients with pain syndromes concurrently with depression. Dr. Eide explained that currently duloxetine is non-preferred for depression but is preferred for fibromyalgia in the Pain, other class. **<u>Stimulants and Related Agents</u>** Dr. Martinez provided a review of Idaho's market share and reported that there are three new generics, dextroamphetamine 5mg/5ml solution for Procentra, clonidine ER for Kapvay and dexmethylphenidate for Focalin XR. Dr. Eide brought up the recent FDA warnings for some of the long-acting methylphenidate generics which are not AB rated. The committee felt that consistency in the product used was the most important factor to consider. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. The PDL document does not currently accurately reflect the correct criteria for Strattera use and needs to be changed. **<u>Sedative Hypnotics</u>** Dr. Martinez provided a review of a new product Hetlioz (tasimelteon), which is indicated for the treatment of non-24-hour sleep wake disorder. She reviewed the clinical trials for this new product. She also announced that there is a new generic eszopiclone for Lunesta. The starting dose for eszopiclone has been decreased from 2 mg to 1 mg for both men and women. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.

➢ *Anticonvulsants*	*Sarah Martinez, PharmD*	**<u>Anticonvulsants</u>** Dr. Martinez announced two new products in this class. Fycompa (perampanel) is indicated as adjunctive treatment for partial-onset seizures, with or without the presence of generalized seizures in patients 12 years and older. Fycompa is a schedule III controlled substance and comes with a black box warning which pertains to serious psychiatric and behavioral reactions. Warnings include neurological effects and suicidal thoughts or behavior. She reviewed the clinical studies used for drug approval. All were placebo-controlled only and perampanel was used as add on therapy in patients receiving one to three concomitant anticonvulsants. The second new product is Aptiom (eslicarbazepine) indicated as adjunctive treatment of partial-onset seizures. Warnings include suicidal behavior and ideation, serious dermatologic reactions, hypersensitivity with eosinophilia and anaphylactic reactions and angioedema. Dr. Martinez then reviewed three clinical placebo-controlled studies for Aptiom. Enrolled patients were not adequately controlled with one to three concomitant antiepileptic drugs. There is a new extended release topiramate preparation - Qudexy XR. It is indicated for initial monotherapy in patients 10 years and older with partial onset or primary generalized tonic-clonic seizures and adjunctive therapy in patients two years and older with Lennox-Gastaut Syndrome. Warnings, adverse effects and drug interactions are similar to those for other topiramate formulations. Topamax's (topiramate) migraine prophylaxis indication has now been expanded to include adolescents 12-17 years of age. Keppra XR (levetiracetam) is now indicated in patients 12 years and older as adjunctive treatment for partial onset seizures (previously approved for ages 16 years and older) and Vimpat (lacosamide) is now indicated as monotherapy in the treatment of partial-onset seizures in patients 17 years and older (previously indicated only as adjunct therapy in this population). Dr. Martinez discussed that the label for Onfi (clobazam) has been revised to include warnings and precautions for serious dermatological reactions including Stevens-Johnson syndrome and toxic epidermal necrolysis. **Committee Recommendations** The committee discussed that this was a broad class without the interchanagablilty as a whole that is seen in the other classes. Most of the adjuvants have specific criteria for use. They concluded that there was no efficacy, effectiveness, or safety evidence to prefer one agent over another within indications.

➢ *Antihypertensives, Sympatholytics*	*Sarah Martinez, PharmD*	**Antihypertensives, Sympatholytics** Dr. Martinez announced no new significant clinical information for drugs in this class, **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between these agents.
➢ *NSAIDS*	*Sarah Martinez, PharmD*	**NSAIDS** Dr. Martinez reviewed the market share information and announced a new product in this class. Zorvolex (diclofenac), which is indicated for the treatment of mild to moderate acute pain in adults and the management of osteoarthritis pain. Unlike other diclofenac products, it is a free acid formulation rather than a salt form. She reviewed the placebo-controlled clinical trials associated with its approval. Pennsaid is now available in a 2% pump and the 1.5% solution is now available as a generic. **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. Because there is a wide choice of preferred agents, it was recommended that failure of more than one preferred agent be implemented if more cost effective.
➢ *Pain Drugs, Other*	*Sarah Martinez, PharmD*	**Pain Drugs, Other** Dr. Martinez announced two new generics, lidocaine patch for Lidoderm and duloxetine for Cymbalta. There was no significant new clinical information to review. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Antihyperuricemics, oral*	*Sarah Martinez, PharmD*	**Antihyperuricemics, oral** Dr. Martinez announced that there is no new significant clinical 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.
➢ *Antiparkinson Agents/Restless Leg Syndrome*	*Sarah Martinez, PharmD*	**Antiparkinson Agents/Restless Leg Syndrome** Dr. Martinez announced one new generic, carbidopa for Lodosyn. Azilect is now indicated as an adjunct to dopamine (previously indicated as monotherapy or adjunct to levodopa). **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Alzheimer's Agents*	*Sarah Martinez, PharmD*	**Alzheimer's Agents** Dr. Martinez 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. They recommended that Namenda XR be preferred only if cost effective.
➢ *Otic Antibiotics*	*Sarah Martinez, PharmD*	**Otic Antibiotics** Dr. Martinez announced that there is no new clinical 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.
➢ *Otic Anti-infectives and Anesthetics*	*Sarah Martinez, PharmD*	**Otic Anti-infectives and Anesthetics** Dr. Martinez announced that there is no new significant clinical 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.

➢ *Other Committee Business*	*Tami Eide, PharmD*	**Other Committee Business** Our next P&T Committee meeting is scheduled for April 17, 2015. Tami will email next year's schedule to all committee members. There is no other committee business. The meeting adjourned at 3:00 p.m.

Pharmacy and Therapeutics Committee
Public Comment
November 14, 2014

Committee
Is Dr. Charles Novak here? Okay, I will come back to him. It looks like we only have one private citizen, and that's Cathy Garrett, who was unable to join us, but submitted some written testimony that will be read in her place, so Chris?

Chris Johnson
So I'm going to be Kathie Garrett for now. You have a copy of this testimony on your desk. So my name is Cathy Garrett, and I am here on behalf of NAMI Idaho. NAMI Idaho is a state organization chartered by the National Alliance of Mental Illness to serve people impacted by mental illness. Thank you for granting us this opportunity to present testimony regarding access to psychiatric medications. We urge you to continue to provide full and open access to psychiatric medications. For many people living with mental illness, access to medication that they and their doctor feel is the right course of treatment is a key component in their health and recovery. Based on the experience of many of our members and families, NAMI Idaho supports full and open access to psychiatric medications and opposes policies, such as restrictive formularies and "fail first" policies. I have a copy of a letter stating NAMI Idaho's official position for the committee. Also, in a new study administered by the National Council for Behavioral Health and NAMI, and published in psychiatric services found that formulary restrictions, prior authorization, and fail-first policies are obstacles significantly affecting mental health outcomes. The study found medication restriction policies directly impact patient wellness. Three-quarters of psychiatric states that the patients had trouble complying with medication plans, while 62% said patients experience increased emergency department visits, hospitalizations, and increased health care costs. Increasing medication options will provide better care and improve patient results, according to those surveyed, and nearly 90% of psychiatrists agree that multiple medication options are important in allowing them to find the best fit for patients based on potential side effects in relation to their condition. The article goes on to state that mental health treatments are not one-size-fits-all. Choosing the right plan should be the decision of the patient and their doctor, not rigid health plan policies. According to NAMI's National Executive Director, the survey confirms what individuals and families affected by mental

illness know from direct experience; having a choice in medication is critical for positive outcomes. I have included the November 6, 2014 press release about the study, and thank you for your consideration.

Committee
Okay, why don't we move on to drug company representatives. So, the first up is Laura Litzenberger from Janssen. If I can ask you to introduce yourself and your role, and then stick to the points please of the testimony that was approved, that would be great.

Laura Litzenberger
Okay, thank you. My name is Laura Litzenberger, and I'm a pharmacist with the Health, Economics and Outcomes Research Group at Janssen Scientific Affairs. Today, I am going to speak on Invega Sustenna. Invega Sustenna is a long-acting, injectable antipsychotic approved for the treatment of schizophrenia, and on Wednesday it received FDA approval for the treatment of schizoaffective disorders, both as monotherapy and as adjunct therapy. I'm going to review two studies today. The first is a pivotal trial in the schizoaffective disorder, and the second is a comparative trial led by the NIMH for comparing Invega Sustenna to Haldol decanoate. So to start out with that, the efficacy of Invega Sustenna to maintain symptom control in schizoaffective disorder was established in a long-term, double blind, placebo-controlled, flexible dose, randomized withdrawal study. Patients were enrolled that had schizoaffective disorder, both of the bipolar and the depressive types. It started off with a 13-week, open-label, Invega Sustenna flexible dose to find a dose to control the acute exacerbation of schizoaffective disorder, and then it was followed by a 12-week open-label, Invega Sustenna period of time where people were stabilized and really to determine if that was a stabilized dose. After that, 334 patients were then randomized either to continue on their Invega Sustenna or to be switched to placebo, that's the withdrawal part, to look at the time until withdrawal, and the risk of relapse in that patient population. So in the patients that remained on Invega Sustenna, the dose of Invega Sustenna in 50% of the patients was 156 mg monthly. The next most common dose was 236 mg and that was in 38% of the patients. There was a statistically significant difference in the time to relapse between the two treatment groups in favor of Invega Sustenna. The risk of relapse was 2.5 times higher in the placebo group than in the Invega Sustenna group. The absolute difference with relapse was seen in 33% of the placebo and 15% of the Invega Sustenna group. There was a 65% reduction in risk of relapse, due to psychiatric symptoms and a 66% risk of relapse, due to mood symptoms in favor of the paliperidone group. The primary reason for relapse was interventions to avert hospitalizations or worsening of clinical scores at two consecutive visits. The most common adverse events in this trial, occurring more frequently in the Invega Sustenna group than in the placebo group were weight increase, headache and insomnia. In the second trial, the ACCLAIM trial, is a comparison of long-acting injectable medications for schizophrenia. It's a double blind, randomized, multicenter, US trial, and, as I said, it was funded by the NIMH. It was comparing the effectiveness of Invega Sustenna to Haldol decanoate for the maintenance of schizophrenia or schizoaffective disorders. The primary outcome was efficacy failure, and that was defined as either a psychiatric hospitalization, need for crisis stabilization, or a clinically meaningful increase in outpatient visits or the clinician's decision that the patient had worsened. Patients were followed for a mean of 15 months. The mean monthly dose of Invega Sustenna after both of these drugs were titrated with oral medication and then switched over to the injectable long-acting, so the mean monthly dose of paliperidone or Invega Sustenna was 129-165 mg compared to the Haldol decanoate dose which was 67-83 mg. There was no statistical difference in the rate of efficacy failure between the two drugs. The most common reason for failure was psychiatric hospitalization or the clinician discontinuing the medication. Compared to Invega Sustenna, Haldol

decanoate was associated with more akathisia and significantly greater use of medications to treat Parkinsonism and akathisia. Invega Sustenna was associated with more weight gain and higher prolactin levels. The authors conclude that in the treatment of patients with schizophrenia or schizoaffective disorder, efficacy was not significantly different between the two groups, but notes that clinical meaningful advantages to Invega Sustenna versus Haldol decanoate cannot be ruled out, due to the differences in dosing. Any questions? Thanks.

Committee
The next person we have is Dr. Jill Kerrick Walker from Neuroscience Medical Science...

Jill Kerrick Walker
That's for when we get to anticonvulsants.

Committee
I'm sorry from Eisai? When we get to anticonvulsants? No, it's, all the private testimony is done.

Jill Kerrick Walker, PharmD
Oh! Forgive me. Okay. I'm Dr. Jill Kerrick Walker, I'm a clinical pharmacist by training, currently with Eisai Medical Affairs, and on behalf of Eisai, I would like to thank you for the opportunity to provide this comment. For 23 years, I've been in the epilepsy practice as a clinician, a published investigator and in Pharma Drug Development. Still, after over two decades and many new compounds, we still have the same percentage of patients with intractable or drug-resistant epilepsy, and over a third of patients who have epilepsy, despite receiving anti-epileptic drug therapy, still experience serious seizures, some of which are catastrophic. Perampanel is indicated for adjunctive therapy, as you know, for partial seizures with or without secondary generalization. This is a key point. This is in patients age 12 and older. Perampanel is the first non-competitive AMPA glutamate receptor antagonist approved by the FDA. Eisai recommends that perampanel be available to beneficiaries with preferred drug status in the Idaho Medicaid program, as it helps to address the unmet need; patients with intractable epilepsy.

So moving on very quickly, perampanel was evaluated in three phase-3 clinical trials. These were patients with partial onset seizures with or without secondary generalization. It is important to keep in mind that these patients were highly refractory, and they could have been receiving one, up to three anti-epilepsy drugs and still having seizures. So for the pooled data for placebo and 2, 4, 8 and 12 mg and our primary endpoints for the percent decline in median seizure frequency, as well as responder rates, these are as follows: For the median change in all seizure frequencies relative to baseline and then placebo was 13% decline, then 2 mg, which is the starting dose, 14% decline, 4 mg 23%, 8 mg 29%, 12 mg 27% decrease. Then moving over to the non-responder rates (again, this is looking at the percentage of patients that achieve at least a 50% or greater decline in their overall seizure frequency, so this is different) placebo was 19%, 2 mg 21%, 4 mg 29%, 8 mg 35% percentage of patients achieved 50% or greater reduction. 12 mg was 35% as well. Currently, perampanel is approved in 40 countries with over 25,000 patients receiving perampanel to date. As you well know, there is a box warning telling our prescribers and patients about the risk of serious and life-threatening neuropsychiatric events, including irritability, aggression, homicidal ideation and hostility, violent thoughts or threatening behavior

were observed in six patients. This is in over 4,000 patients exposed to perampanel. Its dose is a single, once-daily at bedtime. I'm not going to go into the dosing. So in summary, perampanel provides payers, providers and patients with a new FDA option for adjunctive treatment of partial onset seizures in the indicated population. It's orally administered once a day as a single tablet. The other thing is that individualized treatment in this disease state to optimize drug therapy is key. Therefore, Eisai recommends perampanel receive preferred status in the Idaho Medicaid program. Thank you very much for your time.

Committee
Does anybody have any questions? Thank you very much.