Pharmacy and Therapeutics (P&T) Committee Meeting Record

Date: November 18, 2016

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

Moderator: Phil Petersen, M.D.

Committee Members Present: Phil Petersen, MD-Chair; Tami Eide, PharmD; Andrei Rudyi, PharmD; Alex Adams, PharmD, Board of Pharmacy; Christopher Streeter, MD; Paul Driver, PharmD; Perry Brown, Jr., MD; Mark Turner, MD; Stephen Carlson, PharmD; Cali Bradberry, PA; Brian Crownover, MD

Committee Members Absent: None.

Others Present: Sarah Martinez, PharmD, Magellan Health Services; Chris Johnson, PharmD, Division of Medicaid; Jane Gennrich, PharmD, Division of Medicaid; Clay Lord, Division of Medicaid; Keshia Schneider, Division of Medicaid; Mark England, PharmD, Magellan Medicaid Administration

AGENDA ITEMS	PRESENTER	OUTCOME/ACTIONS
CALL TO ORDER	*Phil Petersen, MD*	*Dr. Petersen called the meeting to order.*
Committee Business ➢ *Roll Call*	*Phil Petersen, MD*	Dr. Petersen completed the roll call and welcomed the P&T Committee members.
➢ *Reading of Mission and Confidentiality Statements*	*Phil Petersen, MD*	Dr. Petersen read the Mission and Confidentiality Statements.
➢ *Approval of Minutes from October 21, 2016 Meeting*	*Phil Petersen, MD*	The October 21, 2016 minutes were reviewed. The minutes were accepted with changes from Dr. Brown regarding ophthalmic steroids and oral contraceptives.
Second Generation Antipsychotics in Children Less than 6 years old	*Tami Eide, PharmD*	**Second Generation Antipsychotics in Children Less than 6 years old** Dr. Eide provided a summary of an OIG report (March 2015) on quality of care concerns regarding second-generation antipsychotics in Medicaid-enrolled children. OIG directed CMS to work with state Medicaid agencies on review and oversight. This OIG report found that 67% of the group studied had quality of care concerns.

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<tr><td></td><td></td><td>As a follow-up to the OIG report, Idaho Medicaid in March 2016 reviewed medication profiles of children five years old and younger receiving second generation antipsychotics; 49 children were identified with 82% being male. The predominant antipsychotic prescribed was risperidone (frequency in the sample of 84%); while the predominant presumed indication was autism (frequency in the sample of 39%). Overall, 17 of the children had additional mental health diagnoses, while 38 had one to three additional psychotropics.

An analysis of the presumed indications based on FDA indications CMS approved, compendia, or available quality evidence and guidelines was also completed in the March 2016 study. The results were:

• Supported Indication 27%
• Diagnosis indication met but below age for indication 37%
• Indication not supported 22%
• Unknown Indication 45%

Prescribers were as follows:

• Specialists 29%
• Generalists 27%
• Mid-Level Practitioners 45%

In September 2016, the Medicaid Pharmacy Program asked prescribers for additional information including chart notes on those still receiving second generation antipsychotics that were still under 5 years old.</td></tr>
<tr><td>Public Comment Period</td><td>Phil Petersen, MD
Keshia Schneider</td><td><u>Public Comment Period</u>

Two attendees from the public came to provide testimony, and one of these (Ginny Riley) declined when called to testify.

There were no pre-approved representatives from the pharmaceutical industry.

Public testimony was received from the following speaker:

<table>
<tr><th>Speaker</th><th>Representing</th><th>Agent</th><th>Class</th></tr>
<tr><td>Liza Long</td><td>NAMI</td><td>---</td><td>Antipsychotics in general</td></tr>
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Review of Guidelines for Public Testimony from Pharmaceutical Manufacturers and Their Representatives	*Tami Eide, PharmD*	**Guidelines for Public Testimony from Pharmaceutical Manufacturers** Dr. Eide presented the approved guidelines for pharmaceutical representatives, which are summarized briefly below: • Speakers must submit proposed testimony in writing 15 business days prior to the meeting at which they wish to testify. • Submission must include a one-page summary of 250 words or fewer. • Testimony is restricted to new information not already available to the committee through standard drug information sources that has been published or has been accepted for publication in a peer-reviewed journal since the last review.
Drug Class Reviews and Committee Recommendations	*Sarah Martinez, PharmD* *Magellan Health Services*	**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 comparative evidence to support clinically significant differences in efficacy or effectiveness between agents? If yes, what are the differences? 2. Is there comparative evidence to support clinically significant differences in safety between agents? If yes, what are the differences? 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, Atypical (Second Generation)*	*Sarah Martinez, PharmD*	**Antipsychotics, Atypical (Second Generation)** Dr. Martinez reported on two new oral agents in this class Nuplazid (pimavanserin) and Vraylar (cariprazine) and a new injectable Aristada (aripiprazole lauroxil). She reported on indications, dosing and administration, warnings, drug interactions and adverse effects for each of these agents. Nuplazid is limited to treatment of hallucinations and delusions associated with Parkinson's disease psychosis. She also reviewed the approval trials for cariprazine and pimavanserin. There is no comparative evidence for either new agent. Dr. Martinez reported on the following product and guideline updates: • Invega (paliperidone) is now available generically. • Abilify (aripiprazole) Discmelt and solution are also now available generically. • Rexulti is now indicated for maintenance treatment of schizophrenia in adults (previously indicated only for schizophrenia treatment and adjunct treatment in major depressive disorder). • In May 2016, the American Psychiatric Association practice guidelines mentioned risperidone and olanzapine as having potential drawbacks in terms of adverse effects when used to treat agitation or psychosis inpatients with dementia.

		• In May 2016, the FDA reported that DRESS (drug reaction with eosinophilia and systemic symptoms) will be added to olanzapine labeling (all formulations) as a warning. • The FDA issued a drug safety communication regarding impulse-control problems associated with aripiprazole-containing products including compulsive or uncontrollable urges related to gambling, shopping/spending money, binge eating, and sexual behavior.
➢ *Antipsychotics, Typical*	*Sarah Martinez, PharmD*	**Antipsychotics, Typical** Dr. Martinez reported the following product updates: • Moban (molindone) is now available as a generic. • Orap (pimozide) is now available as a generic. • Adasuve has a boxed warning for provider facilities to have on hand appropriate treatments for bronchospasm. **Committee Recommendations** The committee recommended that fluphenazine be a preferred agent as it is on the World Health Organization list of essential drugs. The committee recommended that thioridazine remain on the non-preferred list for safety concerns. The Committee asked the Department to monitor pediatric use of first-generation antipsychotics for a possible increase in use when criteria for use of the second generation agents make them more difficult to obtain.
➢ *Antidepressants, SSRI*	*Sarah Martinez, PharmD*	**Antidepressants, SSRI** There were no new agents in this class to discuss. The American College of Physicians guidelines for treatment of major depressive disorder which was updated June 2016 does not recommend one antidepressant over another. **Committee Recommendations** The committee recommended that the minimum age for paroxetine be set at 18 years due to evidence that this SSRI is not efficacious in children and adolescents. The committee concluded that other than paroxetine in children, the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Antidepressants, Other*	*Sarah Martinez, PharmD*	**Antidepressants, Other** There were no new agents in this class to report.

		The American College of Physicians guidelines for treatment of major depressive disorder which were updated June 2016 do not recommend one antidepressant over another. The trade name Brintellix has been changed to Trintellix to decrease the risk of prescribing and dispensing errors resulting from name confusion with Brilinta. **Committee Recommendations** The committee recommended making all Monamine Oxidase Inhibitors (MAOI) non-preferred because of safety issues. The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the non- MAOI agents in this class.
Drug Class Review: Second-Generation Antipsychotic Drugs	*Marian McDonagh, PharmD* *Pacific Northwest Evidence-based Practice Center*	**<u>Second-Generation Antipsychotic Drugs</u>** Dr. McDonagh presented evidence regarding this class from the 5th updated report of the class completed October 2016. This report included new comparative evidence plus the addition of aripiprazole (Aristada) ER IM injection, brexpiprazole (Rexulti), cariprazine (Vraylar) clinical evidence. The comparative report now includes 54 studies and 24 companion studies. Regarding patients with schizophrenia: • Clozapine reduced suicides and suicidal behavior, and may improve psychiatric symptoms better than other drugs. • Relapses were less frequent with oral olanzapine, long-acting injectable risperidone, and clozapine. • Olanzapine had lower rates of discontinuation of drug over periods of up to two years, and quality of life or functioning differences were not found across the drugs. • Long-acting injectable risperidone had statistically significantly lower risk of withdrawals due to adverse events. Regarding bipolar disorder: • No significant differences between risperidone or asenapine and olanzapine in quality of life, remission, and response outcomes in adults. • Extended-release paliperidone similar to olanzapine on general functioning and to both olanzapine and immediate-release quetiapine in response or remission rates, but inferior to olanzapine on recurrence rates in adults. • Direct evidence is extremely limited in children and adolescents • Response and weight gain similar between olanzapine and risperidone in preschool-aged

		children. • Only placebo-controlled evidence was found for aripiprazole, extended-release quetiapine, and risperidone. Regarding patients with diagnoses of Autism Spectrum and Conduct Disorders: • Direct comparative evidence is extremely limited • Differences not found between aripiprazole and risperidone for autism spectrum disorder. • Risperidone, aripiprazole, lurasidone, and olanzapine improved behavioral symptoms in autism spectrum disorder versus placebo. • Risperidone and quetiapine showed efficacy in disruptive behavior disorders versus placebo. Regarding Serious Harms: • Quetiapine was associated with lower mortality than risperidone after 6 months in patients with bipolar disorder. • Clozapine was associated with higher risk of myocarditis or cardiomyopathy than other drugs. • Olanzapine was associated with a 16% increased risk of new-onset diabetes and resulted in greater risk of clinically important weight gain compared with other drugs. • Risperidone resulted in a small increased risk of new-onset tardive dyskinesia. • Withdrawal due to adverse events was greater for asenapine than olanzapine in bipolar disorder. • Extrapyramidal symptoms were more frequent with extended-release paliperidone than olanzapine in adult patients with bipolar disorder. • Evidence on other adverse events, including extrapyramidal symptoms and and sexual dysfunction, did not consistently find differences among the drugs. • Evidence on long-term harms for the newest drugs was lacking. **Committee Recommendations** The committee concluded that there was no evidence to support clinically significant difference in efficacy or effectiveness between agents. For safety they concluded olanzapine was worse for metabolic side effects and clozapine for agranulocytosis and orthostasis. The committee recommended making risperidone ODT preferred due to advantages of this dosage form in children. The committee recommended limiting the lower doses of quetiapine to short term titration doses as most other uses were for off label indications such as insomnia. The committee

		recommended also evaluating the number of patients taking quetiapine doses of 800mg or higher. The Committee recommended that second generation antipsychotics be prior authorized in children 5 years or younger. Specific recommendations include: • Require consultation with a child psychiatrist or developmental pediatrician within one month of prescribing if used off label. This could be a telephone consultation. • Physician assistants and nurse practitioners should be working under or in the same office setting as child psychiatrist or developmental pediatrician or have specialized training and qualifications. • Require attestation of informed consent from the parent or guardian and what was included in the informed consent. The informed consent should include a warning of permanent movement disorders. • Require psychosocial treatment prior to and concurrent with drug treatment. • Monitoring requirements per national guidelines including movement disorder scales. • Initial approval no longer than 6 months and then no longer than 12 months.
➢ *Stimulants and Related Agents*	*Sarah Martinez, PharmD*	**<u>Stimulants and Related Agents</u>** There are several new products in this class, including Adzenys XR ODT (amphetamine), Dyanavel XR (amphetamine), and Quillichew ER (methylphenidate). Armodafinil generic for Nuvigil is also available. Dyanavel XR, Quillichew ER and Adzenys XR ODT are all indicated for the treatment of ADHD. **Committee Recommendations** The committee concluded that there was no comparative evidence to support clinically significant differences in efficacy, effectiveness or safety between the agents within the stimulant ADHD drugs, non-stimulant ADHD drugs and drugs for narcolepsy. The committee recommended that both immediate and extended release formulations of methylphenidate and amphetamine be available as preferred as well as a liquid ADHD formulation.

		The committee felt strongly that there should be follow-up on any patients prescribed these agents every 6-12 months. They recommended performing a DUR using Truven data to identify office visits for 2015.
New Public Health Grant for Prescription Drug Overdose Prevention	*Christine Hahn, MD, State Public Health Medical Director*	**New Public Health Grant for Prescription Drug Overdose Prevention** Dr. Hahn reported on a new grant received from the CDC to implement a prescription drug overdose prevention program. She is working with the Office of Drug Policy regarding data collection and analysis. Idaho death certificates document drug overdose as a cause of death, but do not specify which drugs are involved. For that reason, it is not possible to identify deaths due to opiate overdose. Dr. Hahn will also be working with Vital Statistics and the Coroners' Association to develop a training program for coroners to more specifically document which drug the patient overdosed on. Other initiatives covered by the grant funding will involve education and electronic medical improvements through the Board of Pharmacy, Public Health Districts, and Idaho State University.
➢ *Sedative Hypnotics*	*Sarah Martinez, PharmD*	**Sedative Hypnotics** Dr. Martinez announced that Intermezzo (zolpidem sublingual) is now available as a generic. She reported that effective September 2016, a black box warning will be added to all opioid and benzodiazepine-containing product labels stating that concomitant use of opioids and benzodiazepines has resulted in serious adverse effects, including respiratory depression and death. In May 2016, the American College of Physicians released clinical practice guidelines on the management of chronic insomnia disorder in adults. Recommendations include cognitive behavioral therapy for insomnia as the initial treatment. In progressing to pharmaceutical treatment, individual drugs were not recommended. The guidelines mention low-to-moderate data in support of doxepin, eszopiclone, zolpidem, and Belsomra effectiveness. **Committee Recommendations** The committee concluded that there was not comparative evidence to support clinically significant difference in efficacy or effectiveness. They concluded that benzodiazepines, specifically temazepam were more addictive and had more safety concerns than zolpidem.

		The committee recommended that temazepam be non-preferred for safety reasons and that Rozerem be made a preferred agent due to a more favorable safety profile. The committee also made recommendations for PA criteria for use: • Requiring an cognitive behavior therapy for insomnia trial at least annually • Quantity and duration for new patients of 14 doses for 60 days. • Grandfather current patients, but send warning to prescribers of patients on long-term therapy every three months with warnings and need to wean off.
➢ *Anticonvulsants*	*Sarah Martinez, PharmD*	**<u>Anticonvulsants</u>** There were two new agents to report in this class, Spritam (levetiracetam) and Briviact (brivaracetam). Dr. Martinez reviewed Spritam indications, warnings, dosing and adverse effects. There are no contraindications or significant drug interactions. Briviact is indicated as adjunctive therapy in the treatment of partial onset seizures in patients 16 years and older. Dr. Martinez reviewed contraindications, warnings, dosing, and adverse effects. She also reviewed studies used to approve this drug including three fixed-dose, multicenter, randomized, double-blind, placebo-controlled clinical trials. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents within the indications of epilepsy or pain and mood disorders.
➢ *Colony Stimulating Factors*	*Sarah Martinez, PharmD*	**<u>Colony Stimulating Factors</u>** Dr. Martinez reported that are no new products and no recent clinical information of significance in this class. **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*	**<u>Erythropoiesis Stimulating Proteins</u>** Dr. Martinez reported that there are no new products and no recent clinical information of significance in this class.

		Committee Recommendations The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *NSAIDs*	*Sarah Martinez, PharmD*	**NSAIDs** Dr. Martinez reported that Vivlodex (submicronized meloxicam) is the only new product in this class. Contraindications, warnings, adverse effects, and drug interactions are similar to those for other meloxicam products. Dosing is different and Vivlodex is not interchangeable with other formulations of meloxicam. She also reported that Voltaren gel (diclofenac) is now available generically. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy or effectiveness between the agents, but there are some differences in gastrointestinal side effects and cardiac toxicity.
➢ *Pain Drugs, Other*	*Sarah Martinez, PharmD*	**Pain Drugs, Other** Dr. Martinez reported that there were no new products and no recent clinical information of significance in this class. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. They stated that lidocaine transdermal may have a role in decreasing use of opioids in some patients.
➢ *Antihyperuricemics, oral*	*Sarah Martinez, PharmD*	**Antihyperuricemics, oral** Dr. Martinez reported no new products and no recent clinical information of significance 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 that up to 6 tablets of colchicine pay at the pharmacy without prior authorization when needed for the treatment of acute gout.
➢ *Antiparkinson Agents/Restless Leg*	*Sarah Martinez, PharmD*	**Antiparkinson Agents/Restless Leg Syndrome** Dr. Martinez reported no new products and no recent clinical information of significance in

Syndrome		this class. **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 reported the following product updates: • Namenda (memantine) solution is now available as a generic • Exelon (rivastigmine) patch 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.
➢ *Otic Antibiotics*	*Sarah Martinez, PharmD*	**Otic Antibiotics** There are two new agents in this class, Otovel (ciprofloxacin/fluocinolone) and Otiprio (ciprofloxacin). **Committee Recommendations:** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. As Otiprio is instilled by a health care professional during tympanostomy tube placement it will not be covered as part of the outpatient prescription drug program.
➢ *Otic Anti-infectives and Anesthetics*	*Sarah Martinez, PharmD*	**Otic Anti-infectives and Anesthetics** There were no new agents and no recent clinically significant information in this class to report on**.** **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 meeting adjourned at 2:48 p.m. Next meeting will be on April 21, 2017.

Pharmacy and Therapeutics Committee Meeting
Public Comment

Liza Long, Board President, NAMI (National Alliance on Mental Illness) -Boise

Hi, I'm Liza Long. I'm here as a parent, and also as a representative of NAMI-Boise and of NAMI Idaho. I am not receiving any compensation for my testimony, and I am also here primarily as a parent of a child who falls into the category that you're considering today. I am here on behalf of the National Alliance on Mental Illness, Boise and Idaho, where family members and people living with mental illness in our community. As a mother of a son who has bipolar disorder, I am advocating for open access to all medications used to treat mental illness, including antipsychotic medications.

I can understand the concerns that the committee may have, especially in prescribing to this population five and under. As a parent myself, though, I would like you to know that these children are often suffering. We've looked at some of the conditions these children have; my son had a diagnosis of pervasive developmental disorder not otherwise specified, he also had a diagnosis of oppositional defiant disorder and intermittent explosive disorder, and I can tell you that it was not just a child saying, "No." My family experienced violence; my son expressed a desire to die at the age of four. I do believe that doctors should have access to medications that can save lives for children. I applaud the committee for taking reasonable steps to ensure that our children's health is safeguarded, and for monitoring outcomes. Monitoring outcomes in this population is very important because side effects are serious, as we noted, but please do not limit access to medications that can help families and children like mine. Today my son is 17 years old; he is successfully treated, living in the community and I expect that he'll go to college. When he was five, I did not see that future for him, and I am grateful for the opportunity that my family had to access medical care. Thank you.

Dr. Petersen, P&T Committee: If I may ask—you don't have to answer, of course—how old was your son when he first needed medication?

Ms. Long: My son was a little bit older than this population—seven. He started at seven, and he was part of the Medicaid population for part of the time.

Dr. Carlson, P&T Committee: Are there any safety parameters that you would want for children to be monitored as far as their blood sugars or lipids... As a parent, what was your biggest concern that you might be missing?

Ms. Long: The side effects can be serious, and watching the presentation I just saw, I've seen that there was not a consistent standard of care for monitoring physical health including metabolic outcomes, I think as a parent, was my biggest frustration with my son. So having some kind of safeguards in place, some kind of standard procedure in place to ensure that children are being evaluated for their physical health, we really don't know the long-term effects, that's true. But we're talking about a serious illness, that's what I want you to understand. These aren't families just saying, "Oh, I have a bad kid that I don't want to deal with"—these aren't temper tantrums.

Committee: Any further questions for Liza? Thank you very much.