Pharmacy and Therapeutics (P&T) Committee Meeting Record

Date: Friday, October 17, 2014
Time: 9:00 a.m. – 3:00 p.m. **Location:** Idaho Medicaid, 3232 Elder Street, Boise, Idaho, Conference Rooms D-East and D-West

Moderator: Perry Brown, M.D.

Committee Members Present: Perry Brown, MD-Chair; David Calley, PharmD; Tami Eide, PharmD; Troy Geyman, MD; Jeffrey Johnson, PA-C, PharmD; Leigh Morse, MD; Stephen Carlson, PharmD; Mark Turner, MD; Kevin Ellis, PharmD; E. Gregory Thompson, MD

Others Present: Matthew Lennertz, PharmD, Magellan Health Services; Sarah Martinez, PharmD, Magellan Health Services; Mark England, PharmD, Magellan Medicaid Administration; Jane Gennrich, PharmD, Division of Medicaid; 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.
➢ *Reading of Confidentiality and Mission Statements*	*Perry Brown, MD*	Dr. Brown read the Confidentiality and Mission Statements.
➢ *Approval of Minutes from May 23, 2014 Meeting*	*Perry Brown, MD*	The May 23, 2014 meeting minutes were reviewed. Dr. Brown had one edit at the bottom of page 4 and with that edit, Dr. Turner made a motion to accept the minutes, Dr. Morse seconded and the Motion passed. The minutes were accepted as proposed.
➢ *DERP Update*	*Tami Eide, PharmD*	**Drug Evidence Review Project (DERP) Update** Dr. Eide provided an update of the recent DERP governance conference held October 1st and 2nd. Topics up for review to be voted on by the Governance include an ADHD update, Corticotropin (Acthar Gel) review of evidence for indications, ivacafator (Kalydeco) expanded indications and

		an initial comparative review of long-acting insulins. DERP is putting emphasis on drugs in the pipeline including first in class that are either high cost and low volume or high impact clinically or financially; biosimilar agents; or existing drug products with expanded indications, new dosage forms or new combinations of existing drugs. Dr. Eide also discussed information on trends in drug research including new pathways for FDA approval.
➢ *Botulinum Toxins Therapeutic Criteria*	*Jane Gennrich, PharmD*	**Botulinum Toxins Therapeutic Criteria** Dr. Gennrich provided an update on Idaho Medicaid's current therapeutic criteria for botulinumtoxin products. She explained that these medications are covered as a medical claim only and not as outpatient prescriptions as these medications are administered by a physician. Prior authorization was not required prior to July 2013, so there were no restrictions on its use before then. A DUR (drug utilization review) project was done in April 2013 analyzing claims paid between October 1 and December 31, 2012. Current criteria for Botox for migraines for new patients includes documentation that patient is having at least 15 days per month of chronic daily headaches lasting at least four hours and trial and failure of at least two prophylactic medications. Initial approval is for two doses administered three months apart. Additional doses require documentation that Botox has significantly reduced headache frequency and duration. Requests to treat cervical dystonia and spasticity require medical necessity documentation and trial and failure of at least two oral skeletal muscle relaxants. The other FDA approved indications including urinary incontinence were briefly reviewed.
Public Comment Period	*Perry Brown, MD* *Tammy Haugland*	**Public Comment Period** Dr. Perry Brown and Provider Synergies staff reviewed industry submitted scientific information prior to the meeting. Two (2) people signed up to speak during the public comment period. One (1) industry submission was approved for public testimony. Public testimony was received from the following speaker's:

Speaker	Representing	Agent	Class
Kara Garner, NP	St. Luke's Hemophilia Center	All	Hemophilia
Carl Rizo	Self	All	Tobacco Cessation

		Dr. Michael Dutro | Pfizer | Chantix | Tobacco Cessation
Drug Class Reviews and Committee Recommendations	*Perry Brown, MD*	**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?
➢ *Intranasal Rhinitis Agents*	*Matthew Lennertz, PharmD* *Magellan Health Services*	**<u>Intranasal Rhinitis Agents</u>** Dr. Lennertz announced FDA approval of A/B rated generics of azelastine (for Astepro) and budesonide (for Rhinocort Aqua). Nasacort (triamcinolone) is now available over the counter. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. The committee recommended placing OTC Nasacort on the PDL only if it provided a cost-effective advantage over the prescription only agents.
➢ *Cough and Cold*	*Matthew Lennertz, PharmD*	**<u>Cough and Cold</u>** Dr. Lennertz announced that there was no new significant clinical information for drugs in this class. He reviewed utilization of cough and cold preparations for the months of January and September to account for seasonal variation. Utilization for the most part has been for preferred agents. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Tobacco Cessation*	*Matthew Lennertz, PharmD*	**<u>Tobacco Cessation</u>** Dr. Lennertz discussed two new studies within this class. The first study, a randomized, double-blind, placebo controlled, parallel group study was conducted to evaluate the safety and efficacy of retreatment with varenicline in adults smokers who previously attempted to quit with varenicline. The continuous abstinence rate was significantly higher in varenicline patients than

		in placebo patients. The second study was conducted to determine if smokers diagnosed with schizophrenia, schizoaffective disorder or bipolar disorder have higher rates of prolonged abstinence with maintenance pharmacotherapy of varenicline plus cognitive behavioral therapy than with standard cognitive behavioral therapy alone. It was pointed out that the endpoint measurement in this study was done at 52 weeks and varenicline is only FDA approved for 24 weeks of therapy. Dr. Lennertz announced that the application to remove the black box warning on Chantix for serious neuropsychiatric events was not approved by the FDA. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. It was recommended that if non-nicotine replacement agents (i.e. systemic agents) had similar cost effectiveness that they be available as preferred agents.
➢ *Antihistamines, minimally sedating*	*Matthew Lennertz, PharmD*	**<u>Antihistamines, minimally sedating</u>** Dr. Lennertz announced that there was 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.
➢ *Oral Anti-allergens*	*Matthew Lennertz, PharmD*	**<u>Oral Anti-allergens</u>** This is a new PDL drug class for review. Dr. Lennertz provided a brief overview of allergic rhinitis and current treatment which includes antihistamines, corticosteroids, and subcutaneous allergen specific immunotherapy (SCIT). This class represents an alternative allergen specific immunotherapy, sublingual allergen immunotherapy or SLIT. Sublingual oral anti-allergens in this class include Grastek (Timothy grass pollen extract) and Ragwitek (ragweed pollen allergen extract). Dr. Lennertz discussed pharmacology, administration and contraindications of these agents. He reviewed the clinical trials associated with the FDA approval of each agent. **Committee Recommendations** The committee discussed the products available and commented on the various grass varieties in Idaho. The committee recommended that both agents be available through prior authorization depending on grass species in Idaho. PA requirements should include a positive allergen-specific

		test and failure of a minimum of 8 weeks of therapy with antihistamines and an intranasal corticosteroid. The committee recommended that a full year of medical history be required for prior authorization review. The pharmacy unit is to research the specific allergy season for these allergens in Idaho and restrict use to that season including the designated time period required prior to the beginning of the season.
➢ *Epinephrine, self-injected*	*Matthew Lennertz, PharmD*	**Epinephrine, self-injected** Dr. Lennertz announced that there was 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 and that preferred status should be based on cost-effectiveness.
➢ *Drugs to Treat Asthma and Chronic Obstructive Pulmonary Disease*	*Shelly Selph, MD Pacific Northwest Evidence-based Practice Center*	**Drugs to Treat Asthma and Chronic Obstructive Pulmonary Disease** Dr. Selph reviewed the evidence report for drugs to treat asthma and chronic obstructive pulmonary disease. Drugs she reviewed included inhaled corticosteroids (ICS), long-acting Beta-2 agonists (LABA), leukotriene modifiers, long-acting anticholinergics, phosphodiesterase-4 inhibitors and combination products. She indicated that the overall findings did not suggest that a single medication within any of the classes evaluated is significantly more effective or harmful than the other medications within the same class. Results supported the general clinical practice of starting initial treatment for persistent asthma with an ICS. For people with poorly-controlled persistent asthma taking an ICS, the evidence suggested that the addition of a LABA is most likely to provide the greatest benefits as the next step in treatment. For patients with COPD, the results indicated that monotherapy with ICS and LABAs are similarly effective and have similar risk for any adverse event. However, there was low-strength evidence that treatment with ICS increased the risk of serious pneumonia in these patients.
➢ *Bronchodilators, Beta Agonists*	*Matthew Lennertz, PharmD*	**Bronchodilators, Beta Agonists** Dr. Lennertz reviewed one new product in the long-acting inhalation product class, Striverdi Respimat (olodaterol). It is indicated for the treatment of airflow obstruction in patients with COPD, including chronic bronchitis and/or emphysema. He reviewed the clinical trials associated with this agent.

		Committee Recommendations The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents within the short-action inhalation, long-acting inhalation and oral agent sub-classes. They specifically did not feel that there were any advantages to the new long-acting agent Striverdi. The committee discussed issues with electronic medical records which automatically default to brand name Ventolin, even though the prescriber has no preference for which albuterol product is used (generic albuterol not an option). The Board of Pharmacy is to be contacted to see if there are any way interchangeability can be allowed.
➢ *Leukotriene Modifiers*	*Matthew Lennertz, PharmD*	**<u>Leukotriene Modifiers</u>** Dr. Lennertz announced that an FDA panel has recommended rejecting an application to move montelukast to OTC status. There was no new significant clinical information to review. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Glucocorticoids, Inhaled*	*Matthew Lennertz, PharmD*	**<u>Glucocorticoids, Inhaled</u>** Dr. Lennertz announced two new products in this class. Aerospan (flunisolide) is indicated for maintenance treatment of asthma in patients six years and older and in asthma patients where adding flunisolide may reduce or eliminate the need for oral steroids. Breo Ellipta (fluticasone/vilanterol) is indicated for the long term maintenance treatment of airflow obstruction in patients with COPD, including chronic bronchitis and/or emphysema. He reviewed the clinical trials for these agents. Neither have comparative data with other drugs in the class available for review. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *COPD Agents*	*Matthew Lennertz, PharmD*	**<u>COPD Agents</u>** Dr. Lennertz announced that Anoro Ellipta (umeclidinium/vilanterol) has been approved by the FDA. This drug is indicated for the long-term, once-daily, maintenance treatment of airflow obstruction in COPD patients. He also reviewed the updated guidelines and recommendations from the 2014 Global Initiative for Chronic Obstructive Lung Disease (GOLD).

		Committee Recommendations The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents within the subclasses of anticholenergics and anticholinergic-Beta agonist combinations. The committee asked that the definition of "severe" COPD be clarified in the prior-authorization criteria.
➢ *Immune Globulins*	*Matthew Lennertz, PharmD*	**<u>Immune Globulins</u>** Dr. Lennertz announced that Octagam 10% is now indicated for chronic idiopathic thrombocytopenic purpura in adults. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. There was some concern on the safety of subcutaneous preparations, but the committee also felt that it would be desirable to have at least one subcutaneous preparation available if cost effective.
➢ *Botulinum Toxins*	*Matthew Lennertz, PharmD*	**<u>Botulinum Toxins</u>** Dr. Lennertz provided an overview of this new drug class. Botulinum toxins are used to treat a variety of medical conditions including: cervical dystonia, upper arm spasticity, severe axillary hyperhidrosis, blepharospasm, treatment of strabismus, prophylaxis of headaches in adults with chronic migraine, urinary incontinence due to detrusor over activity and overactive bladder. Botox Cosmetic in indicated for temporary cosmetic improvement of glabellar lines and lateral canthal lines. Cosmetic use is not covered by Medicaid. Dr. Lennertz reviewed the differences in indications between the products. He also reviewed the clinical trial information for Botox vs. Dysport and Botox vs. Myobloc in cervical dystonia. **Committee Recommendations** The committee concluded that within common indications by product that the evidence did not support differences in efficacy, effectiveness or safety between the agents. They recommended prior authorization be maintained for all agents. For migraine use they recommended that the criteria require the failure of two prophylactic and two abortive agents and a neurological consult.

➢ *Targeted Immune Modulators*	*Kylie J. Thaler, MD, MPH RTC-UNC Evidence-based Practice Center*	**Targeted Immune Modulators** Dr. Thaler presented the May 2014 DERP review of targeted immune modulators. Included in the criteria for the review were the following populations: rheumatoid arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, psoriatic arthritis, Crohn's disease, ulcerative colitis and plaque psoriasis. Only head to head trials of at least 12 weeks duration were used in the study criteria. Overall, Dr. Thaler said that data from highly-selected and short-term randomized trials in patients with rheumatoid arthritis provides evidence on comparative efficacy and shows that the efficacy of the targeted immune modulator drugs is similar. For plaque psoriasis, ustekinumab is more efficacious than etenercept. Most direct evidence on the comparative harms of targeted immune modulators exists for rheumatoid arthritis and for patients receiving adalimumab, etanercept, and infliximab. Overall, where differences in harms between the drugs were detected, infliximab is associated with a greater risk of serious adverse events, serious infections and withdrawal due to adverse events.
➢ *Cytokine/CAMS*	*Matthew Lennertz, PharmD*	**Cytokine/CAMS** Dr. Lennertz announced the FDA approval of additional indications for four products in this drug class. Actemra was approved in a single use prefilled syringe for subcutaneous injection. Simponi is now indicated for the treatment of moderate-to severe ulcerative colitis in adults. Humira is now indicated for reducing signs and symptoms and achieving and maintaining clinical remission in patents six years and older with moderately to severely active Crohn's disease that have had an inadequate response to conventional therapy. Cimzia is now indicated for treatment of adult patients with active psoriatic arthritis and treatment of adults with active ankylosing spondylitis. There are three new products approved since the last review. Entyvia (vedolizumab) is indicated for the treatment of moderately to severely active ulcerative colitis or Crohn's disease in patients with an inadequate response or intolerability to a TNF blocker, immunomodulator or who have intolerance or dependence on corticosteroids. Otezla (apremilast) is indicated for the treatment of adult patients with active psoriatic arthritis and moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy. IIaris (canakinumab) is indicated for the treatment of active Systemic Juvenile Idiopathic Arthritis (SIJA) and Cryopyrin-Associated Periodic Syndromes (CAPS). Dr. Lennertz reviewed clinical trials for these agents. There was no comparative data with any of these agents. **Committee Recommendations** The committee stated that tocilizmab may have efficacy advantages for rheumatoid arthritis and infliximab for Crohn's Disease. There are definite safety issues with infliximab. It was

		recommended that infliximab be available first line for Crohn's Disease without requirement of failure of a preferred agent. Apremilast as a new agent may have advantages safety wise with no demyelination, CNS, or PML side effects. Oral administration may also be an advantage.
➢ *Hemophilia Agents*	*Matthew Lennertz, PharmD*	**Hemophilia Agents** This is a new PDL drug class. Dr. Lennertz gave an overview of the disease state and treatment recommendations. Hemophilia, regardless of type, is classified as mild, moderate or severe depending on the intrinsic amount of clotting factor, in the patient's blood. The recommended treatment of bleeding episodes is dependent on several factors including the patient's severity level, the location and type of the injury or trauma as well as the patient's overall status. Providing immediate treatment reduces the risk of lasting damage, the need for additional medication, the reduction of pain as well as additional treatments. Most of the trials with agents in this class were performed in an open-label manner. No direct comparisons have been done and therefore no conclusions regarding the comparative safety or efficacy can be made. Dr. Lennertz then reviewed the different Factor products and their recommendations for treatment. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents within each Factor group. The committee recommended having one recombinant and one plasma derived product for Factor VIII and Factor IX. They recommended that bypassing agents be available. They recommended that anyone on a current agent be grandfathered and not be required to change products.
➢ *Immunomodulators, Atopic Dermatitis*	*Matthew Lennertz, PharmD*	**Immunomodulators, Atopic Dermatitis** Dr. Lennertz reviewed updated guidelines published by the American Academy of Dermatology with recommendations for atopic dermatitis. There was 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.
➢ *Steroids, Topical*	*Matthew Lennertz, PharmD*	**Steroids, Topical** Dr. Lennertz reviewed agents and utilization in the subclasses of very high potency, high potency, medium potency and low potency. New products in the very high potency class include Clodan (clobetasol) and Temovate ointment, a new ointment formulation of clobetasol. New products in the medium potency class include Dermatop cream (prednicarbate), Clocortolone, an authorized

		generic for Cloderm cream and a generic hydrocortisone butyrate (for Locoid Lipocream). **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. The committee recommended having a representation from each potency and preparation available.
➢ *Ophthalmic Antibiotics*	*Matthew Lennertz, PharmD*	**<u>Ophthalmic Antibiotics</u>** Dr. Lennertz reviewed the drugs in this class and their utilization. He announced that the FDA had approved an A/B rated generic gatifloxacin (for Zymaxid). **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Ophthalmic Antibiotic/Steroid Combinations*	*Matthew Lennertz, PharmD*	**<u>Ophthalmic Antibiotic/Steroid Combinations</u>** Dr. Lennertz reviewed the drugs in this class and their utilization. There was 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.
➢ *Ophthalmics, Anti-inflammatories*	*Matthew Lennertz, PharmD*	**<u>Ophthalmic, Anti-inflammatories</u>** Dr. Lennertz reviewed the drugs in this class and their utilization. There was 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.
➢ *Ophthalmics for Allergic Conjunctivitis*	*Matthew Lennertz, PharmD*	**<u>Ophthalmics for Allergic Conjunctivitis</u>** Dr. Lennertz reviewed the drugs in this class and their utilization. There was 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.
➢ *Ophthalmics, Glaucoma Drugs*	*Matthew Lennertz, PharmD*	**Ophthalmics, Glaucoma Drugs** Dr. Lennertz reviewed the drugs in this class and their utilization. There was 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 within the subclasses of parasympathomimetics, sympathomimetics, beta blockers, carbonic anhydrase inhibitors, prostaglandin analogs and combination agents.
➢ *Idaho Medicaid Hepatitis C Update*	*Chris Johnson, PharmD*	**Idaho Medicaid Hepatitis C Update** Dr. Johnson provided an overview of current Hepatitis C treatment evidence and Idaho's current clinical guidelines for treatment and prevention of Hepatitis C. He included the prior authorization criteria for sofosbuvir which was approved by the P&T Committee on May 23, 2014. Dr. Johnson provided an overview of the number of treatment requests (47), number approved (10) and number denied (37). For those approved, he reviewed the number by genotype and break down of patients by those completing treatment, in active treatment and those who did not start or complete treatment. He also reviewed the characteristics of those not meeting criteria which in general was a too low fibrosis level and/or active drug or alcohol abuse. Dr. Johnson then reviewed the newer Hepatitis C drugs in the pipeline and their expected approval dates.
➢ *Other Committee Business*	*Tami Eide, PharmD*	**Other Committee Business** Our next P&T Committee meeting is scheduled for November 14, 2014. There was no other committee business. The meeting adjourned at 3:00 p.m.

Pharmacy and Therapeutics Committee
Public Comment
October 17, 2014

Kara Garner, NP

My name is Kara Garner, I'm a nurse practitioner, I'm with the St. Luke's Hemophilia Treatment Center. I'm representing the Hemophilia Treatment Center today, and I have no financial ties. So, thank you very much for allowing me to speak today. I came here. St. Luke's is the only Federally funded hemophilia treatment center in the state of Idaho, so my responsibilities include the entire state of Idaho for anybody with a bleeding disorder, which includes von Willebrand's and all factor deficiencies. We have currently in the world of hemophilia, there is quite a bit going on. We have many projects that are in the works right now. Currently, there is the ATHN, the American Thrombosis and Hemostasis Network, that currently has several projects. One is their universal data collection, which has never been done with bleeding disorders throughout the United States. We are participating in that. Currently, there is about a third of the country that is enrolled with My Life, Our Future, and within this, there is a third of the population throughout the state, and they have currently found over sixty new mutations within hemophilia, so that's very exciting for the world of hemophilia. There are many new products on the market that there has been very thorough research being done on, and I appreciate that, that all of the products have been thoroughly researched and properly represented. I wanted to come here today to also offer if there were any questions with regards to hemophilia, the clinical aspects, and offer our expertise to share with Medicaid to help align ourselves with your goals. We also have the same goals that we are interested in, so thank you very much.

Carl Rizo

Hello, my name is Carl Rizo. I am a respiratory therapist. I guess I work for St. Luke's Saltzer. I really am not getting reimbursed for doing this. I really have no pharmaceutical ties. I really came today to talk about smoking cessation. Last year, I did come down and talk to you a little bit about that, and it was my information, the information I gave you last year was based more on gut feeling and "this is what's been happening", but this year I have a little bit more data. This year, basically, what I came back with is over the last year I have seen 302 patients for smoking cessation. What I have found is that in the data that I received back from those patients, over 55% of those patients did not need any medication at all to quit smoking. I truly believe that education is the primary component that we need to use. Most people that I talk to do not understand, or have not been given any information, so "thank you Millennium Fund". So we're out there doing that. I will say that in many cases, if people come to the conclusion that they do want to use a medication, I will recommend that they go ahead and use the Millennium Fund, that's directly what that's set up for. I have run into about, I guess it's about 5% of patients that actually came back that said that they could not use the nicotine replacement therapy, that the education alone wasn't doing it, and they did come to the conclusion that they had to use something else. I see bupropion is one of

the medications on there. All that I'm asking is that all medications be available equally across the board. The reason being, I'm an ex-smoker, I smoked for 27 years and was really good at it. What I really found was that people that smoke, it's very personal, and when they want to quit, that becomes very personal too, so whatever they need to use is what they need to use. There's really no other way around that, and if they believe that is the only way they're going to quit, then that is the only way they're going to quit. Again, though, I have been keeping a fair amount of data, just so that I'm not speaking from the hip basically. That is all I really came to offer, just that we offer things across the board. Any questions? Thank you.

Michael Dutro, MD
Thank you. I'm Dr. Michael Dutro from Pfizer Medical Affairs, here to update you on varenicline or Chantix. The following two studies in recent label updates that we were asked to present are not included in the Magellan Review of Smoking Cessation Agents. Let me define two terms that I'll use throughout my presentation: When I say "AE's" I mean "adverse events" and when I say "Quit rates", I mean carbon monoxide-confirmed continuous abstinence rates for the time period that I describe.

So the first study: Most smokers require multiple attempts to permanently quit smoking. In a study to evaluate re-treatment with varenicline in 494 smokers who previously had taken it, participants were randomized to varenicline or placebo for twelve weeks. Quit rates were significantly higher for varenicline for weeks 9-12 (45% versus 12%) and weeks 9-52 (20% versus 3%). AE's with varenicline re-treatment were similar to previous trials involving patients naive to varenicline.

The next study is one of the largest done to evaluate smoking cessation with patients with schizophrenia. It was published earlier this year in JAMA by independent researchers. It evaluated varenicline with intensive behavioral treatment for relapse prevention in 203 patients with stable, treated schizophrenia or bipolar disease. All patients received open-label varenicline for twelve weeks. The 43% who were able to quit were then randomized to either varenicline or placebo. The quit rates were significantly higher for varenicline for weeks 12-52 (45% versus 15%) and weeks 12-76 (30% versus 11%). Twenty-six randomized patients prematurely discontinued. However, sensitivity analysis conducted by the authors demonstrated it had no effect on the significance of the results. Although the study involved a sample size which limited its ability to estimate risk of serious AE's, there were no significant treatment effects on psychiatric symptom scales or psychiatric adverse events.

We've had a couple of label updates with important new information in the last month, including one that occurred yesterday, and we have copies of the new label for anybody who would like it. In 2009, varenicline received a box warning concerning risk of serious neuropsychiatric events that is still current. It recommends that patients stop taking varenicline and contact a health care provider if they experience agitation, hostility, depression, or changes in behavior or thinking, including suicidal behavior. The box warning is

based on spontaneous adverse events reported to the FDA. The FDA recently approved several updates to the varenicline label, including new data that further evaluate the neuropsychiatric safety profile of this medication. The updated profile includes results from a Pfizer meta-analysis of five clinical trials that showed no increased risk in the incidence of suicidal ideation or behavior with varenicline compared with placebo. It also included results of a Pfizer pooled analysis of eighteen clinical trials which showed a similar incidence of the common psychiatric events of anxiety, depressed mood or other mood disturbances in patients treated with varenicline compared with placebo. In addition, the label now contains results from four independently-conducted, large, observational studies, each of which included from 10 to 30,000 varenicline patients with and without a psychiatric history. The studies assess the risk of selected, serious neuropsychiatric events between varenicline and either NRT or bupropion. Two additional warnings were added to the label; one for worsening of seizures and one for an interaction with alcohol. In addition, data from two randomized clinical trials were added to the label: The first was a study that evaluated re-treatment with varenicline that I presented previously, and the second was a placebo-controlled trial in 525 patients with major depression, either currently stably treated or with a recent past history. Subjects treated with varenicline had superior quit rates for weeks 9-12 versus placebo (36% versus 16%) and for weeks 9-52 (20% versus 10%). Psychiatric scales showed no differences between varenicline and placebo, and no overall worsening of depression, and similar rates with suicidal ideation or behavior between the groups. Individual psychiatric adverse events occurring in over 2% were also included in the label. The body of evidence supports the first-line use of varenicline along with support as an aid to smoking cessation. It has been studied in smokers with a variety of comorbidities, including COPD, cardiovascular disease, depression and schizophrenia. It has been shown to be effective, with a favorable benefit/risk ratio. We respectfully ask that varenicline be added as a preferred PDL agent for first-line therapy, with no prior authorization. Does anybody have any questions? Thank you.