Pharmacy and Therapeutics (P&T) Committee Meeting Record

Date: Friday, May 10, 2013 Time**:** 9:00 a.m. – 3:00 p.m. **Location:** Idaho Medicaid, 3232 Elder Street, Boise, Idaho, Conference Room D

Moderator: Perry Brown, M.D.

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

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

AGENDA ITEMS	PRESENTER	OUTCOME/ACTIONS
CALL TO ORDER	Perry Brown, M.D.	Dr. Brown called the meeting to order.
Committee Business		
➢ *Roll Call*	*Perry Brown, M.D.*	Dr. Brown completed the roll call, welcomed the P&T Committee members and called the meeting to order.
➢ *Reading of Mission Statement*	*Perry Brown, M.D.*	Dr. Brown read the Mission Statement.
➢ *Approval of Minutes from April 19, 2013 Meeting*	*Perry Brown, M.D.*	The April 19, 2013 meeting minutes were reviewed. Dr. Thompson moved to accept the minutes, Dr. Turner seconded and the Motion passed. The minutes were accepted as proposed.
➢ *DERP Update*	*Tami Eide, PharmD*	Dr. Eide gave an overview of the DERP Work Plan-Year 2, for July 2012-June 2013. Report topics include ADHD Treatments in Adults, Combination Report on Asthma and COPD, Diabetes Drugs, Oral Oncology Drugs and Targeted Immune Modulators.

➢ *Update on Growth Hormone in Prader Willi Syndrome*	*Jane Gennrich, PharmD*	Dr. Gennrich gave an update on Growth Hormone in Prader Willi Syndrome which was presented at the previous P& T Committee meeting. The material submitted by two parents of Prader Willi children was reviewed by Dr. Gennrich, Dr. Perry Brown, and Dr. Paula Townsend. The committee decided that the level of evidence of the materials submitted (including journal articles and abstracts from a national Prader Willi Conference) does not support changing Idaho Medicaid's current therapeutic criteria for growth hormone.
➢ *DUR Board Update: Migraine Prevention – Prophylaxis Utilization in Chronic Triptan Utilizers*	*Mark England, PharmD*	**DUR Board Updates – Migraine Prevention – Prophylaxis Utilization in Chronic Triptan Utilizers** Dr. England gave an overview from the DUR Board meeting regarding migraine prevention. Idaho Medicaid paid over $777,000 in pharmacy claims for the Triptan class in 2012. He discussed the epidemiology and the type of recipients with paid claims. The report shows that there are more females than males using migraine medications. The information also showed that there was a 10% increase globally in incidence of migraine from 1989 to 1999. In 2012, Idaho Medicaid had 5022 unique recipients with a migraine diagnosis in their electronic medical records and of these 5022 recipients, 1258 had at least one paid triptan claim in their profile.
➢ *Narcotic Analgesic Update*	*Tami Eide, PharmD*	**Narcotic Analgesic Update** Dr. Eide gave an update on Medicaid's initiatives for improving the use of opioids in chronic non-malignant pain. She reviewed the information from the original DUR study in 2011 for 30 participants receiving over 500 mg morphine equivalents per day and the results of a follow-up study on these same 30 participants in 2013. Only 6 of the 30 patients are still receiving over 500mg/day morphine equivalents. The Committee discussed multiple issues including methods to stop participants from paying cash for additional opioids over what Idaho Medicaid has paid for and locking in participants to one prescriber for opioids if they are on greater than a certain threshold of morphine equivalents daily. The committee voted to set a threshold of 300 mg morphine equivalents per day and to require lock-in and prior authorization over that threshold. The committee would like to have Mark Johnston, RPh, with the Board of Pharmacy do a presentation about the current work being done by the Board of Pharmacy about opioid abuse and diversion.

Commented [ETJ-M1]: Increase In what?

<table>
<tr>
<td>Public Comment Period</td>
<td>Perry Brown, M.D.
Cody Scrivner</td>
<td><u>Public Comment Period</u>
Three (3) people signed up to speak during the public comment period. 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>Dr. Jim Herrold</td><td>Idaho Medicaid Provider</td><td>All MS Drugs</td><td>Multiple Sclerosis Agents</td></tr>
<tr><td>Caleb Simpson</td><td>Self</td><td>Novantrone, Tysabri,</td><td>Multiple Sclerosis Agents</td></tr>
<tr><td>Jessica Alexander</td><td>TEVA Neuroscience</td><td>Copaxone</td><td>Multiple Sclerosis Agents</td></tr>
</table>
</td>
</tr>
<tr>
<td>Drug Class Reviews and Committee Recommendations</td>
<td></td>
<td>Drug Class Reviews and Committee Recommendations</td>
</tr>
<tr>
<td>➢ Analgesics, Narcotic long-acting</td>
<td>Paula Townsend, PharmD
Magellan Health Services</td>
<td><u>Analgesics, Narcotic long-acting</u>
Dr. Townsend reviewed a new indication for Nucynta ER for pain associated with diabetic peripheral neuropathy. The FDA Actions in this class are for (1) Opana ER (oxymorphone ER) – the label has been updated to include a warning for thrombotic thrombocytopenic purpura resulting in kidney failure when this drug is crushed and then injected and (2) Oxycontin (oxycodone ER) which has been reformulated with physical properties that are expected to make abuse via injection and nasal inhalation difficult and therefore the FDA announced it will not be approving any new ANDA's (generics) for the original formulation.

Committee Recommendations
The Committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents and that preferred status should be based on cost-effectiveness. The Committee also endorsed continuing the Department's current therapeutic criteria.</td>
</tr>
<tr>
<td>➢ Analgesics, Narcotic short-acting</td>
<td>Paula Townsend, PharmD</td>
<td><u>Analgesics, narcotic short-acting</u>
Dr. Townsend gave an update on one new product/formulation in this class -Subsys which is a fentanyl sublingual spray indicated for breakthrough cancer pain in patients who have developed</td>
</tr>
</table>

		tolerance to other opioid medications. It is not equivalent to other sublingual/buccal fentanyl products. Brand name Vicodin (hydrocodone/acetaminophen) has been re-formulated so that each tablet contains 300 mg acetaminophen. **Committee Recommendations** The committee recommended moving butorphanol nasal spray from preferred to non-preferred status because of safety and addiction issues. They recommended limiting the amount of daily acetaminophen doses by making combination products with higher amounts of acetaminophen non-preferred. The Committee concluded that other than these recommendations that the evidence did not support differences in efficacy, effectiveness, or safety between the other agents and that preferred status should be based on cost-effectiveness.
➢ Opiate Dependence Treatments	Paula Townsend, PharmD	**<u>Opiate Dependence Treatments</u>** Dr. Townsend provided a review of one new indication for treatment of alcohol dependence for oral naltrexone tablets,. New generics available are naltrexone tablets (ReVia) and buprenorphine/naloxone generic tablets (for Suboxone). **Committee Recommendations** The Committee recommended designating oral naltrexone tablets as preferred on the Preferred Drug List. The Committee concluded that the evidence does not support differences in efficacy, effectiveness, or safety between the other agents and that preferred status should be based on cost-effectiveness. The Committee also recommended continuing the current therapeutic criteria for these agents which includes not paying for other opioids for participants receiving medication for opiate dependence/abuse treatment.
➢ Skeletal Muscle Relaxants	Paula Townsend, PharmD	**<u>Skeletal Muscle Relaxants</u>** Dr. Townsend announced that carisoprodol's (Soma & generics) label will now reflect its new Schedule IV reclassification. It was reclassified in 2011 but not fully implemented and reflected until February 2013. **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.

➢ Antimigraine Agents	Paula Townsend, PharmD	**Antimigraine Agents** Dr. Townsend announced that Maxalt and Maxalt MLT are now available generically as rizatriptan and rizatriptan ODT. **Committee Recommendations** The Committee recommended placing rizatriptan on the preferred drug list for children 6 years and over as this is the only triptan with FDA approval down to age 6 years. The Committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents and that preferred status should be based on cost-effectiveness. The Committee would like the DUR to continue to evaluate preventative therapy in participants having more than 4 migraines per month and consider developing clinician educational guides.
➢ Antiemetics/Antivertigo Agents	Paula Townsend, PharmD	**Antiemetics/Antivertigo Agents** Dr. Townsend reviewed the information from two new clinical trials. A Phase III crossover study comparing aprepitant in combination with a 5HT3 antagonist and dexamethasone in patients with testicular cancer receiving cisplatin combination chemotherapy regimens demonstrated less emesis episodes when aprepitant was given at the beginning of the first chemotherapy regimen.The second trial she reported on showed no difference between various combinations of palonsetron, granisetron, aprepitant, dexamethasone and prochlorperazine. **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. There was also discussion that it would be cost prohibitive to remove criteria for ondansetron.
➢ Ulcerative Colitis Agents	Paula Townsend, PharmD	**Ulcerative Colitis Agents** Dr. Townsend announced a new product in this class - Giazo (balsalazide) which is indicated for the treatment of mildly to moderately active ulcerative colitis (UC) in male patients only. Effectiveness in female patients was not demonstrated in the clinical trials. **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.

➢ H. Pylori Treatment	Paula Townsend, PharmD	**H. Pylori Treatment** Dr. Townsend announced that this is a new drug class to be reviewed by the P&T Committee. She reviewed the most recent (2007) national treatment guidelines Failure rates are increasing and the primary reason is H. pylori resistance to clarithromycin **Committee Recommendations** The Committee recommended that Helidac (metronidazole, bismuth subsalicylate, and tetracycline) and Pylera (bismuth subcitrate potassium, metronidazole, and tetracycline) be available as first line agents as tetracycline is not currently available as a single entity.
➢ Immunosuppresives, Oral	Paula Townsend, PharmD	**Immunosuppressives, Oral** Dr. Townsend announced that Zortess is now approved for liver transplant patients (non-inferiority study as compared to mycophenolate). **Committee Recommendations** The Committee concluded that Zortress should remain non-preferred and that there were no evidence based differences to support preferring any other agent over another in this class and that preferred status should be based on cost-effectiveness
➢ Colony Stimulating Factors	Paula Townsend, PharmD	**Colony Stimulating Factors** This is a new class for P&T Committee review. Dr. Townsend reviewed indications and efficacy data for the individual agents. Limited comparative data suggests that filgrastim and peg-filgrastim have similar efficacy and tolerability and are superior to sargromastim. Filgrastim is typically administered daily while peg-filgrastim is administered once per cycle of chemotherapy. **Committee Recommendations** The Committee asked that patient access be considered in the Department's decision, but concluded that there were no evidence based differences to support preferring any agent over another in this class and that preferred status should be based on cost-effectiveness.
➢ Multiple Sclerosis Agents	Paula Townsend, PharmD	**Multiple Sclerosis Agents** Dr. Townsend announced one new oral drug in this class – Aubagio (teriflunomide) which is indicated for relapsing forms of MS to reduce the frequency of exacerbations. She reviewed clinical trials for teriunomide as well as its adverse drug reaction profile. Rebif is now available as Rebif Rebidose, a prefilled auto injector. Ampyra (dalfampridine ER) now has an FDA

Commented [ETJ-M2]: Where are the guidelines from?

		mandated warning for anaphylaxis and severe allergic reactions. Tecfidera is another new oral MS agent but it was just recently approved by the FDA and did not meet the cutoff for data analysis by Provider Synergies so it will not be reviewed by this committee until next year. **Committee Recommendations** The Committee discussed the new drugs and how that can be accessed by patients. The Committee expressed concern on the efficacy of teriflunomide compared to other agents and recommended making it non-preferred. Tecfidera will be on the PDL as a not-reviewed agent and therefore will require prior authorization. The Committee recommended that Ampyra, which is FDA approved to improve walking and not to decrease the number of relapses, should continue to have therapeutic criteria. The Committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the injectable agents and that preferred status should be based on cost-effectiveness.
➢ Coronary Vasodilators	Paula Townsend, PharmD	**<u>Coronary Vasodilators</u>** Dr. Townsend announced that this is a new drug class to be reviewed by the P&T Committee. She discussed the various product formulations, indications, and dosing. **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 and availability within each administration route formulation. The Committee recommended including at least one dinitrate and one mononitrate formulation as preferred agents..
➢ Antibiotics, Inhaled	Paula Townsend, PharmD	**<u>Antibiotics, inhaled</u>** Dr. Townsend announced that there was no new significant clinical information for this drug class. **Committee Recommendations** The committee recommended keeping both agents as preferred for Cystic Fibrosis patients.
➢ Cephalosporins and Related Agents	Paula Townsend, PharmD	**<u>Cephalosporins and Related Agents</u>** Dr. Townsend announced one new product - Suprax chewable tablet (cefixime). She reviewed the IDSA (Infectious Disease Society of America) new treatment guideline that recommends amoxicillin-clavulanic acid over amoxicillin alone as first-line empirical therapy for children with acute rhinosinusitis without penicillin allergy.

		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.
➢ Fluroquionolones, oral	Paula Townsend, PharmD	**Fluroquinolones, oral** Dr. Townsend announced that levofloxacin has a new FDA approved indication for the treatment of plague, including pneumatic and septicemic. **Committee Recommendations** The Committee recommended that ciprofloxacin suspension be preferred for children with Cystic Fibrosis. The Committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the other agents and that preferred status should be based on cost-effectiveness.
➢ Macrolides/Ketolides	Paula Townsend, PharmD	**Macrolides/Ketolides** Dr. Townsend discussed a revised safety warning in the labeling for azithromycin (Zithromax). Azithromycin can cause prolonged cardiac repolarization and QT interval prolongation, increased risk of cardiac arrhythmia and *torsades de pointes.* She reviewed the IDSA guideline update which recommends that macrolides not be empirically used for acute bacterial rhinosinusitis due to high resistance rates. She also reviewed the 2012 CDC update for the treatment of uncomplicated gonorrhea which includes ceftriaxone plus either azithroumycin or doxycycline. **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.
➢ Tetracyclines	Paula Townsend, PharmD	**Tetracyclines** Dr. Townsend announced that the FDA continues to report that doxycycline is only available in limited supply and that tetracycline is unavailable. The CDC has recommended additional alternative regimens for some sexually transmitted diseases where doxycycline is currently recommended (e.g. chlamydia, nongonococcal urethritis, epididymitis, PID and syphilis) as an alternative in penicillin allergic patients.

		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 and market availability.
➢ Antibiotics, Gastrointestinal	Paula Townsend, PharmD	**<u>Antibiotics, Gastrointestinal</u>** Dr. Townsend announced that this is a new class for review by the P&T Committee. This class of antibiotics treats C. difficile associated diarrhea, Giardia lamblia, Cryptosporidium, Traveler's diarrhea, parasitic infections, bacterial vaginosis, Trichomoniasis and they are also used as part of surgical bowel preparations. She referred to the chart of agents and indications in the therapeutic drug class review document. A new generic, vancomycin HCL oral capsules for Vancocin is now available. **Committee Recommendations** The committee recommended that Alinia, metronidazole, oral vancomycin, and neomycin be preferred and Dificid be non-preferred. The Committee recommended that Xifaxan should have therapeutic criteria in addition to being non-preferred.
➢ Antibiotics, Topical	Paula Townsend, PharmD	**<u>Antibiotics, Topical</u>** Dr. Townsend announced that Bactroban cream is now available generically as mupirocin cream. **Committee Recommendations** The Committee recommended that mupirocin ointment be preferred as it is the drug of choice for impetigo. The Committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the other agents and that preferred status should be based on cost-effectiveness.
➢ Antibiotics, Vaginal	Paula Townsend, PharmD	**<u>Antibiotics, Vaginal</u>** Dr. Townsend announced that there is no new clinical evidence for review. **Committee Recommendations** The Committee recommended that at least one clindamycin and one metronidazole product be preferred.

➢ Antifungals, Oral	Paula Townsend, PharmD	**Antifungals, Oral** Dr. Townsend announced one new drug - Onmel tablets (itraconazole 200mg), which is indicated for treatment of onychomycosis of the toenail. She reviewed dosing and clinical trials of this product. **Committee Recommendations** The Committee recommended that itraconazole (generic) and griseofulvin be preferred if not cost-prohibitive.
➢ Antifungals, Topical	Paula Townsend, PharmD	**Antifungals, Topical** Dr. Townsend announced new over the counter products - Desenex (clotrimazole)andfour new miconazole products - Azolen, Fungoid, Fungoid-D and Zeasorb. In addition there are five new prescription products: Ciclodan (ciclopirox) cream and solution, Pedipirox-4 (cliclopirox) solution, Ketodan (ketoconazole) and Pediaderm-AF(nystatin) . Oxistat (oxiconazole) cream is now FDA approved for the treatment of tinea versicolor. **Committee Recommendations** The Committee recommended that nystatin/triamcinolone combination product be non-preferred due to concerns over using a topical steroid on a fungal infection. The Committee recommended that the DUR board analyze the age breakdown on paid claims for this combination product. The committee concluded that the evidence did not support differences in efficacy, effectiveness, or safety between the other agents and that preferred status should be based on cost-effectiveness.
➢ Antiparasitics, Topical	Paula Townsend, PharmD	**Antiparasitics, Topical** Dr. Townsend reviewed the new drug Sklice (ivermectin lotion) for the treatment of head lice in patients older than 6 months. She review the 2012 Red Book (American Academy of Pediatrics) Guideline for treating head lice. **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.

➢ Antivirals, Oral	Paula Townsend, PharmD	**Antivirals, Oral** Dr. Townsend announced that Tamiflu (oseltamivir) is now FDA approved down to the age of 2 weeks for treatment of patients with acute uncomplicated influenza have been symptomatic for no more than two days and for prophylaxis in patients one year or older. She reviewed the 2012-13 Influenza Guidelines which report high rates of resistance to amantadine and/or rimantadine with emerging resistance to oseltamivir. There was no new significant clinical information to review for the antiherpetic drugs. **Committee Recommendations** The Committee recommended that Tamiflu remain preferred. The Committee also recommended that amantadine be available as a preferred agent without prior authorization as the majority of use for this medication is for conditions other than influenza.
➢ Antivirals, Topical	Paula Townsend, PharmD	**Antivirals, Topical** Dr. Townsend announced a new product Xerese, which is a combination of acyclovir and hydrocortisone cream indicated for early treatment of recurrent herpes labialis to reduce the likelihood of ulcer development. Generic Zovirax Ointment (acyclovir) was approved 4/9/2013. **Committee Recommendations** The Committee recommended that all agents in this drug class be non-preferred with therapeutic criteria.
➢ Other Committee Business	Tami Eide, PharmD	**Other Committee Business** Dr. Eide discussed the amount of work and paper involved in providing paper copies of the PDL and the TCRs (therapeutic class reviews) for all of the members of the P&T Committee. The Committee members agreed that they like having paper copies of the Agenda and PDL and the slides but that they do not need paper copies of the TCRs. The suggestion was that anything that can be posted to the website should be and if there is something submitted at the last minute, then a paper copy of that information should be available to the Committee members at the meeting. The next P&T Committee meeting is scheduled for October 11, 2013. The meeting adjourned at 3:00 p.m.

Pharmacy and Therapeutics Committee
Public Comment
May 10, 2013

James M. Herrold, MD

Good morning, my name's Jim Herrold, I'm a board certified neurologist. I've been in practice here for nearly seventeen years. I'm here just to address some of the issues of multiple sclerosis patients and the medications that are available for them. MS has gotten more and more complicated. It has more drugs come on board and the decision on which drugs to put patients on is sort of like a car salesman deciding Honda, Ford, Toyota, etc. With this disease, 85% of the patients have relapsing-remitting multiple sclerosis, and the drugs that we use do not cure the disease. They essentially cut down on the number of relapses and, secondarily, reduce disability. As you all know, MS can be a pretty devastating disease if it's not aggressively treated, so in summary, I'll just kind of tell you how I approach a patient and explain the drugs to them in terms of efficacy and safety. So the basic drugs that we have are disease-modifying therapies. Copaxone is subcutaneous every day, and then there are interferon drugs, Rebif, Betaseron and Avonex. So those are the two main classes, and those are kind of the stable, standby, "been around for a while" medications. They're all injectable. The interferons have flu-like side effects for some patients. Copaxone has less side effects, but it's a daily subcutaneous injection and some patients have some injection site reactions. The newer class of drugs, finally, have oral medications. There are now three oral medications; Aubagio, which has a little less efficacy than other drugs that I mentioned and also is Category-X in terms of pregnancy issues, that drug's probably not going to be very popular because MS, just like migraine, is more common in women of child bearing age. Then there's Gilenya that's been out for a while, and it is a good drug, except it does have some cardiac issues, so that we don't give it to cardiac patients or those on beta blockers. There have been some cardiac deaths. The newest, greatest thing is a drug called BG-12 or dimethyl fumarate, or the brand name, which is Tecfidera. I explain the drugs, those initial drugs, the Copaxone and the interferon drugs, they reduce annual relapse rate by about 30%, so I put those on a kind of 30% relapse reduction level. The oral drugs are more like 45% or 50% reduction, and then I think the best drug out there is Tysabri, and it's administered intravenously once a month. The big issue with Tysabri, of course, is PML, which is progressive multifocal leukoencephalopathy (PML) and you see it in AIDS patients and what have you, but we're now able to screen patients by checking a JC virus antibody, and half of the people in this room are positive and carry a JC virus antibody, and it's usually benign. It hangs out in your kidneys and does nothing, unless you get immunosuppressed or are on a certain drug. So half the patients are going to be JC virus negative, and if they have moderate to aggressive MS, I'll put them on Tysabri, and that's the best drug out there. I don't really think we should be forcing patients to take platform therapy of Copaxone or Avonex or Rebif, waiting for them to have a relapse and lose the ability to see out of one eye or strength in the leg or bladder, or get some sort of disability, and then once, and only then, do we advance them to a more aggressive therapy. I think, I don't know what the costs are for these, but it seems to me that they are all quite expensive, but they're all roughly the same. So at my practice, if a patient is JC virus antibody negative, I'll advocate for intravenous Tysabri if they have moderate or severe disease, but the Committee should just be aware that going forward, I think the oral medications are going to be taking over a good portion of MS therapy, because I just think, and this is my opinion, but if I offer you a shot with a big needle or a little needle, or any sort of needle versus a pill, I think the preference is going to be on oral medications. My personal choice on the oral medications is going to be Tecfidera. It's brand new, FDA-approved a couple weeks ago, maybe it's been a month ago, and it's called dimethyl fumarate, and there's an analogous drug called Fumaderm that they still use in Europe for psoriatic arthritis, so it has a big track record being used for psoriatic arthritis, and so there shouldn't be

a lot of surprises in terms of side effects. Again, the efficacy for Copaxone and interferons is 30% reduction, the oral medications are 45% or 50%, and Tysabri is about 65% reduction in relapses. If I were to exclude any drugs from the formulary, I'd probably exclude Betaseron because we already have a high-dose interferon in the form of Rebif, which is three times per week versus Betaseron which is a daily injection, and then in the orals, I think Aubagio, which is category-X for pregnancy, it has more like 20-25% reduction in relapse, so it's less efficacious, so that one may be eliminated, and then preferentially I'd choose Tecfidera because of the safety profile over Gilenya. Gilenya patients have to get seen by Ophthalmology before they start the drug and then a few months later to look for macular degeneration, which occurs in about 1 in 500 on the drug. They've got to get a baseline EKG, and then when you administer the drug, the first dose of the Gilenya, they have to follow up for heart rate and blood pressure, because it can induce bradycardia, so it's a good drug, but it's much more complicated and can cause lymphedema too. So, that's my two cents. Are there any questions?

Committee
Yes, Dr. Herrold, do you use, or is there, I'm sure there's data to guide on initial severity of the initial event. I know we've changed over the last decade from necessarily multiplicity of time and location to, you know, more MRI-based, to give you a sense if it's a mild and then resolving MS or MS-like syndrome. Would you, perhaps, go with these newer medicines, or would you consider starting with one of the tried and true Copaxone, etc., and then [inaudible]?

James Herrold, MD
Yes, I'd try to assess the severity based on MRI, so get a brain MRI and if it has a lot of enhanced lesions and looks aggressive, and you're going to want to do more aggressive therapy, but you know, I think in terms of having patients fail platform therapy and then earn the stripe to go on more aggressive drugs, it doesn't make sense if the more efficacious drugs are safe, and I think Tecfidera, the oral medication, is going to be super safe, and Tysabri is only, many practitioners cannot write a prescription, you have to, you know, it's very tightly regulated, and then we have this JC antibody that we can screen patients and follow them for PML, so I think we should be able to use more aggressive drugs for moderate to severe. I think if it's mild MS, that most of the time people will be okay on a basic platform therapy, but cost wise, if the Committee is concerned about cost, and I don't know that the older drug are cheaper, the Copaxone and the Avonex and Rebif, so price being equal, put me on a stronger drug if I have MS, as long as it's safe. I think that's kind of a subjective opinion of a neurologist in terms of the severity of the disease, but I don't think we should reserve, for instance Tysabri or Gilenya or Tecfidera for just people who have horribly aggressive disease. The idea is, it's preventative maintenance. It's sort of like you wouldn't use an inferior blood pressure medication if you knew it led to heart attack and stroke. You'd give them a good, aggressive blood pressure medication. Same thing with MS. Yes?

Committee
Just a quick question. Have you been seeing in the community, the use of the newer oral drug?

James Herrold, MD
No. Because of the PML scare that came with Tysabri, we know that when we start mixing and matching immunosuppressive therapies that bad

things can happen, so I don't think there are any clinical studies that advocate combination therapy of, say, Tysabri and Avonex, or, they may at some point combine therapies which, in my opinion, they'd have to really show good, powerful results, because the cost of the medications as it is with one drug, $3,000 or $4,000 a month, and then if you're on two drugs it's $8,000 times twelve, that's $100,000 a year. You have to think, what's a practical means of treating MS or cancer, but it can be debilitating, so there may be some combination therapy in some patients, but right now, pretty much that's one of the questions you get back when you want to start someone on Tecfidera or whatever, and you'll get a thing back "Is the patient taking any other MS drugs?" and if you say "Yes", pretty much all of the insurances will deny combination therapy.

Committee
Well, it's investigational is why, but there are a number of add-on trials, at least with Aubagio, so I was just wondering if you had seen that.

James Herrold, MD
I'm not aware of any studies that have proven the efficacy of combination therapy, and I think you read a list of immunosuppressing patients and getting opportunistic infections, but yeah, I think for more aggressive patients, I'm all for, you know, aggressive therapy, but your average patient, I don't know, I think we're doing pretty good with. I mean, the oral medications, as I said, we have an oral MS drug that reduces relapses 50%, which is huge, and we've got Tysabri which reduces relapses 65%, so we're doing pretty good with MS, as far as getting people diagnosed and on appropriate therapy.

Committee
Aside from the disease-modifying agents - Ampyra, what are your thoughts on it?

James Herrold, MD
Ampyra somehow gets, the last I was here, Ampyra was on the immune modulating drug...

Committee
It's not.

James Herrold, MD
I hope it's not, still. Ampyra's kind of labeled the "walking drug" and it kind of facilitates, it got FDA approved based on a timed walk of, I think 25 feet, and um, you know, it's an okay drug, I think it's worth, the people that we use that in have gait disorders. They're walking around with canes or walkers or so forth, and I think it's efficacious in half the patients, and I think it's a legitimate drug to try with patients, and if they do see improvement, keep them on it, but certainly if they don't, get them off. So sometimes insurance companies will say "What is the timed walk initially?" "12 seconds" and then you go on the drug and then retest them and see if they walk quicker. That's still very subjective, depending on the patient's effort and so forth, so I think it's kind of a, that's not really the greatest measure, but yeah, I have some patients who have gait disability and they're on Ampyra and it didn't really work, and I'd pull them off quick. What's the point because it's a fairly expensive drug. But

there is some suggestion that maybe it helps with fatigue and heat tolerability. It's not been indicated for that, but um, so I think it's case by case. I wish it weren't so expensive, because that, in combination with immune modulatory therapy gets the prices up, but I think, so I think screening the right patients and allowing those who have significant gait disorders to be on that drug is reasonable, because it sometimes makes the difference between them being able to go grocery shopping and not, so... Thanks.

Caleb Simpson

That's my doctor. I'm Caleb Simpson. I was diagnosed with multiple sclerosis back in 1997. I am a licensed, I was a freshman in college at that time, and I knew that health insurance was going to be a major part of my life, so I studied up on it when I was in college and my first job when I got out of college was selling health insurance. So that's what I'm still doing today, helping a lot of people find health insurance. A lot of Medicare people are my clients, and I spend a lot of time with that. A lot of them are disabled and on Medicaid, so I want to say thank you to the people in this room, the board, the city and the state, for making Medicaid possible. It's a huge help to a lot of my clients. My feedback, basically, I was basically going to say similar things in a less expert way as my doctor, which was that my personal testimony of the drugs was that I started on betaseron and that's one of the first four, the CRAB drugs, Copaxone, Rebif, Avonex and betaseron, that he said are, you know, good, standby and they have 30% efficacy in reducing the rates of relapse by about 30%. But that didn't work very well for me. For eight years, I just stayed on the same one, the betaseron one, that he kind of poo-pooed, I was glad to hear. It works for some people. It didn't work for me, and I ended up basically in and out of a wheelchair in 2005. My MS had progressed that bad. At that point, I switched to one that he didn't mention, which is a chemotherapeutic drug for MS that's not as popular right now with all the new ones, but it's called Novantrone, and that switch changed my life. It's a temporary thing, you can only be on it for a limited, it's chemotherapy, so once you have your lifetime maximum, you've had enough poison and you're done for the rest of your life. But I went from having 2-4 attacks per year all the way down to zero attacks per year, and just living a normal life. When I got done with the chemo, I got on that Tysabri, and it continued that success of zero attacks every year. It was exciting. And then further studies, he talked about how regulated that Tysabri is, and one of the regulations is that they did a new study that anybody who moved from a chemotherapeutic drug like Novantrone to Tysabri is instead of 1 in 1,000 or so, and these, I'm not approved to say these numbers, but I'm a private citizen, but instead of 1 in 1,000 getting PML, it goes down to something like 1 in 60 or 80 or something, and Dr. Herrold was like, "Let's get you off this" because my chances were so much higher, and I was positive for the JC virus. Anyway, I am now on one of the oral medications, so I'm basically a sample of what he was saying. I'm on one of the oral medications and it's continuing that success of having zero. My request, therefore, is please leave it up to the doctors who know all of the drug treatments and know the patients and what's going to be best for them, and not make some step therapy program where you have to try these first, one of these three or four, and fail, and then you can try one of the more aggressive ones. So I just wanted to say, basically the same. Thank you very much.

Jessica Alexander

Thank you for the opportunity to speak. My name is Jessica Alexander. I have a PhD in Neuroscience, and I am here representing Teva Neuroscience. I am not receiving compensation apart from my salary I suppose. Okay, so as you know, I'm providing rationale for maintaining Copaxone on the formulary, and on your preferred drug list. Copaxone is glatiramer acetate 20 mg subcutaneously daily, and it is indicated for the reduction of the frequency of relapses in patients with relapsing-remitting MS, including patients who have experienced the first clinical episode,

so clinically isolated syndrome. So first I'll review the new data that I provided to speak today, and one of these trials is CombiRx. It was a three year, NIH-funded study to evaluate whether or not the combination of interferon plus Copaxone, in this case it was Avonex plus Copaxone, had added benefit versus either agent alone. So patients were randomized in a 2:1:1 design to receiving the combination or one active agent with a matching placebo. So patients received eight injections weekly. This was a three-year trial with a primary end point of analyzed relapse rate. Copaxone treatment led to fewer relapses than Avonex. The combination of Copaxone and Avonex was not superior to Copaxone, and that's the way the trial was designed; to compare the combination to the superior agent alone. However, the combination was superior to Avonex, and a higher portion of Copaxone-treated patients completed the trial, so fewer patients terminated the trial. Also, I submitted information for the PreCISe extension trial. PreCISe was a trial evaluating Copaxone in CIS, so clinically isolated syndrome. In this comparison of clinically isolated syndrome patients randomized to receive Copaxone, it was about 200 patients in each group, or those initiating Copaxone in the open label phase, the time to conversion to clinically definite MS was evaluated, and early Copaxone treatment reduced conversion risk by 41% versus delayed treatment. It was associated with an approximately three-year delay in conversion to clinically definite MS, less brain atrophy, so a 28% reduction in brain atrophy compared to delayed treatment, fewer new T2 lesions per year, lower T2 lesion volume, and lower annualized relapse rate versus delayed treatment. Those papers were published just recently, in December of 2012, for the PreCISe trial, and in February of 2013 for the CombiRx trial. Since I have some additional time, I will just say that there are no available head-to-head studies evaluating Copaxone versus the new oral agents, and in trials that have been conducted against interferons, there is no difference in efficacy, apart from what you may take from the CombiRx trial data. It was approved in 1996 by the FDA, and has a unique mechanism of action. Most of these drugs work at the level of the blood-brain barrier, whereas Copaxone affects the immune cell phenotype in the periphery. It still permits entry to the immune cells to survey the CNS. It is associated with clinically significant and sustained reductions in relapse rate. Trials have been ongoing since it's the longest continuous prospective investigation of an MS...

Committee
I'm going to just stop you here.

Jessica Alexander
You know all this.

Committee
Yeah, the information that we're able to get about the general substances is, you know, we get it through the inserts and through the updates and everything, but the reason that we ask for pharmaceutical representative input are areas specifically where we don't have some of the data from the newer trials, and we really appreciate your presenting that, so did you have anything else to add, or can we open this up for questions?

Jessica Alexander
No. Yes.

Committee
Does anyone have any questions about the data that was presented?

Jessica Alexander
Thank you.

Committee
Thank you very much.