Pharmacy and Therapeutics (P&T) Committee Meeting Record

Date: Friday, May 23, 2014
Time: 9:00 a.m. – 3:45 p.m. **Location:** Idaho Medicaid, 3232 Elder Street, Boise, Idaho, Conference Room D

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

Others Present: Paula Townsend, PharmD, Magellan Health Services; Mark England PharmD, Magellan Medicaid Administration; Jane Gennrich, PharmD, Division of Medicaid; Chris Johnson, PharmD, Division of Medicaid; Cody Scrivner, CPhT, 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 April 18, 2014 Meeting*	*Perry Brown, MD*	The April 18, 2014 meeting minutes were reviewed. Dr. Geyman made a motion to accept the minutes, Dr. Calley seconded and the Motion passed. The minutes were accepted as proposed.
➢ *DERP Update*	*Tami Eide, PharmD*	**DERP Update** Dr. Eide provided an update from the Drug Effectiveness Review Project (DERP). The Evidence-based Practice Center is currently working on a summary report on Hepatitis C treatment. This will include an evaluation of the evidence in recent systematic reviews and

		provide an assessment of gaps in the evidence. This will be available in mid-July. An original systematic review will be completed in February 2015 and updates are scheduled for every 6 months thereafter.
➢ *Update on Growth Hormone Guidelines*	*Jane Gennrich, PharmD*	**Update on Growth Hormone Guidelines** Dr. Gennrich provided an update on the guidelines for growth hormone. Drs. Turner, Eide and Gennrich met with Dr. Daniel Flynn, pediatric endocrinologist. They reached some conclusions on areas of agreement and Dr. Flynn is to supply evidence for Department review for other treatment issues that the Department and he disagree on. Dr. Eide and Dr. Gennrich consulted with the Deputy Attorney General and the initial determination is that being short is not considered a functional impairment and does not meet the American Disability Act guidelines.
➢ *Drug Utilization Review: Oseltamivir/Zanamivir*	*Chris Johnson, PharmD*	**Drug Utilization Review: Oseltamivir/Zanamivir** Dr. Johnson provided an overview of a study of the anti-influenza drugs oseltamivir and zanamivir. This DUR report from 2014 evaluated use of these drugs during the 2012-2013 flu season. The study attempted to correlate usage of the drugs with receipt or non-receipt of the flu vaccine. It was also noted that there was some out of season utilization and that some recipients received more than one prescription. Although 84% of the recipients potentially did not receive flu vaccine, there were several limitations to drawing a definite conclusion to this. Recipients can receive free vaccine through several programs and billing to Medicaid may not consistently only use the specific billing codes. Considerations include education on the importance of vaccination for prevention rather than treating once infected and considering an edit limiting to one time use, only during the flu season.
Public Comment Period	*Perry Brown, MD* *Cody Scrivner*	**Public Comment Period** Dr. Perry Brown reviewed the Scientific Information prior to the meeting and no pharmaceutical representatives were approved to speak. Three (3) people signed up to speak during the public comment period. Public testimony was received from the following speaker's:

Speaker	Representing	Agent	Class
Jim Herrold, MD	Self		Multiple Sclerosis
Tracy Young, NP	Self		Hepatitis C
Stephen Asher, MD	Self		Multiple Sclerosis

Drug Class Reviews and Committee Recommendations		**Drug Class Reviews and Committee Recommendations** Committee members were asked to base their recommendations for each drug class on the answers to the following questions: 1. Is there evidence to support clinically significant differences in efficacy or effectiveness between agents? 2. Is there evidence to support clinically significant differences in safety between agents? 3. Are there any agents that the committee feels strongly must be preferred or non-preferred? 4. Are there any recommendations for changes to PA requirements?
➢ *Idaho Sofosbuvir (Solvadi) and Simeprevir Guidelines*	*Chris Johnson, PharmD*	**<u>Idaho Sofosbuvir (Solvadi) and Simeprevir (Olysio) Guidelines</u>** Dr. Johnson provided an overview of Idaho Medicaid's proposed clinical guidelines for simeprevir (Olysio) and sofosbuvir (Sovoldi). These guidelines include the inclusion and exclusion criteria as well as required medical information and treatment and monitoring documentation to be submitted. These guidelines will be the basis for Idaho Medicaid coverage decisions for these drugs. He reviewed reasons for Department denial of drug coverage for any patient.
➢ *Hepatitis C Agents*	*Paula Townsend, PharmD* *Magellan Health Services*	**<u>Hepatitis C Agents</u>** To put Hepatitis C (HCV) treatment into perspective, Dr. Townsend reviewed the natural history of HCV infection. She reviewed clinical data on two new drugs. Simeprevir (Olysio) is a protease inhibitor indicated for chronic hepatitis C genotype 1 infection. It is not to be used as monotherapy, but in combination with peginterferon alfa and ribavirin. Her review included pivotal clinical trials of simeprevir. The second new drug, sofosbuvir (Sovaldi), is an NS5B polymerase inhibitor. She also reviewed the pivotal clinical trials for sofosbuvir. Dr. Townsend reviewed the information from the American Association for the Study of Liver Diseases (AASLD) treatment guidance document. She reviewed the information from the Medicaid Evidence based Decisions Project (DERP's sister organization) that concluded that studies from the AASLD guidelines had poor methodological quality, risked bias and lacked comparison to current standards of treatment.

		Committee Recommendations Key discussion points by the Committee included fibrosis levels for which there should be treatment, determining alcohol and drug abuse, and the lack of comparative evidence for the drugs based on the significant cost for the therapy. The Committee approved the proposed prior authorization criteria, asked the Department to fine tune the criteria as more experience was gained and to bring the criteria and information on use back to the October P&T meeting for further discussion.
➢ *Antivirals, Oral*	*Paula Townsend, PharmD*	**Antivirals, Oral** Dr. Townsend announced that there was no new significant clinical information. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. They recommended changing rimantadine to non- preferred status based on the high level of resistance to this antiviral.
➢ *Antivirals, Topical*	*Paula Townsend, PharmD*	**Antivirals, Topical** Dr. Townsend announced that Xerese (acyclovir 5%/hydrocortiosone 1% cream) was now indicated for ages 6 and over. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Antibiotics, Inhaled*	*Paula Townsend, PharmD*	**Antibiotics, Inhaled** Dr. Townsend reviewed the information regarding the new products in the class. She reviewed the information around Bethkis, generic tobramycin solution and TOBI Podhaler She reviewed the Cystic Fibrosis Pulmonary Guidelines, "Chronic Medications for Maintenance of Lung Health " that were updated in April 2013. Dr. Brown discussed continuous alternating therapy (CAT) using monthly alternation of tobramycin and aztreonam for certain patients. He also discussed the effect of delivery method on patient compliance.

		Committee Recommendations The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. The committee recommended moving TOBI Podhaler to preferred status if it was cost effective.
➢ *Antibiotics, Topical*	*Paula Townsend, PharmD*	**<u>Antibiotics, Topical</u>** Dr. Townsend indicated that there is no new significant clinical information. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. The Medicaid Pharmacy Unit was asked to brainstorm methods to educate pharmacists and prescribers to enable substitution of mupirocin ointment for mupropion cream with minimum "hassle" and interruption of care.
➢ *Antibiotics, Vaginal*	*Paula Townsend, PharmD*	**<u>Antibiotics, Vaginal</u>** Dr. Townsend indicated that there is no new significant clinical information for drugs in this class. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Cephalosporins and Related Agents*	*Paula Townsend, PharmD*	**<u>Cephalosporins and Related Agents</u>** Dr. Townsend announced that a new product formulation, Suprax (cefliximе) in capsule form was now available and that the Suprax tablet formulation has been discontinued. Cedax is now available generically as ceftibuten in capsule and suspension forms. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Fluroquinolones, Oral*	*Paula Townsend, PharmD*	**<u>Fluroquinolones, Oral</u>** Dr. Townsend announced that a new generic moxifloxacin for Avelox was available and that there is no new significant clinical information.

		Committee Recommendations The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Macrolides/Ketolides*	*Paula Townsend, PharmD*	**<u>Macrolides/Ketolides</u>** Dr. Townsend announced that there was no new significant clinical information. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Tetracyclines*	*Paula Townsend, PharmD*	**<u>Tetracyclines</u>** Dr. Townsend indicated that the FDA continues to report that tetracycline is unavailable and that the doxycycline shortage has been resolved. **Committee Recommendations** Pharmacists on the committee reported that they are still experiencing difficulties in obtaining doxycycline. The committee recommended that the DUR Board review the usage and determine if PA criteria would be appropriate for doxycycline considering the large increase in price over the past year and potentially ongoing shortages. There is a concern of high utilization for acne when alternatives, especially topical agents could be used. There is a significant need for education in other infections as prescribers are still under the impression that it is a cost effective alternative to other drugs such as azithromycin.
➢ *Antibiotics, Gastrointestinal*	*Paula Townsend, PharmD*	The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. **<u>Antibiotics, Gastrointestinal</u>** Dr. Townsend 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. The committee recommended that the current prior authorization criteria for Xifaxin be continued.

➢ *Antifungals, Oral*	*Paula Townsend, PharmD*	**Antifungals, Oral** Dr. Townsend announced a new product, posaconazole delayed-release tablet (Noxafil). Indications include prophylaxis of invasive Aspergillus and Candida infections in severely immunocompromised patients 13 years and older that are at high risk of developing these infections. The oral suspension has been and is still available for this indication plus treatment of oropharyngeal candidiasis, including oropharyngeal candidiasis refractory to itraconazole and/or fluconazole. Voriconazole generic suspension is now available for Vfend. Dr. Townsend reviewed the information from an FDA safety communication for oral ketoconazole. The July 2013 communication limits the use of this drug to severe systemic infections due to its ability to cause severe liver injury and adrenal insufficiency and its potential for harmful drug interactions. The committee discussed the recently updated prior authorization criteria. **Committee Recommendations** Other than safety concerns surrounding ketoconazole, the committee concluded that there were no differences in efficacy, effectiveness or safety between the agents.
➢ *Antifungals, Topical*	*Paula Townsend, PharmD*	**Antifungals, Topical** Dr. Townsend reviewed clinical data on a new product, luliconazole (Luzu), an azole antifungal. It is indicated for treatment of interdigital tinea pedis, tinea cruris and tinea corporis caused by *Trichophyton rubrum* and *Epidermophyton floccosum* in patients 18 years of age and older. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Antiparasitics, Topical*	*Paula Townsend, PharmD*	**Antiparasitics, Topical** Dr. Townsend announced that Elimite (permethrin 5% cream) indicated for the treatment of scabies and first marketed in October of 2012 is now part of this drug class market basket. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Irritable Bowel Syndrome*	*Paula Townsend, PharmD*	**Irritable Bowel Syndrome (IBS)** Dr. Townsend announced that this is a new drug class for the committee and reviewed the clinical information including pharmacology and indications for losetron, linaclotide and lubiprostone.

		She reviewed the NICE (National Institute for Health and Clinical Evidence) 2012 clinical practice guidelines and the AGA (American Gastroenterological Association) 2002 medical position statement on IBS. These guidelines recommend dietary changes and laxatives for mild- to moderate symptoms and reserving linaclotide and luiprostone for moderate-to-severe symptoms. **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. They recommended that PA criteria be continued and that over the counter laxatives be tried first.
➢ *Oral Buprenorphine Drug Utilization Review*	*Jane Gennrich, PharmD*	**<u>Oral Buprenorphine Drug Utilization Review</u>** Dr. Gennrich provided an overview of the ongoing oral buprenorphine drug utilization review that uses the Board of Pharmacy Prescription Monitoring Program to monitor patients paying cash for opioid analgesics while being treated for opiate dependence with buprenorphine or buprenorphine/naloxone. Prescribers are contacted when concurrent use of buprenorphine and opioids is identified. Most prescribers have been appreciative of this information.
➢ *Narcotic Analgesic Prescribing Improvement Project*	*Tami Eide, PharmD*	**<u>Narcotic Analgesic Prescribing Improvement Project</u>** Dr. Eide described the action plan to implement the P&T Committee and DUR Board recommendations for improving narcotic utilization. This is a timeline that will be provided to all prescribers and covers activities from January 2014 through August of 2015. Participants with cancer or other chronic malignant pain syndromes will not be subject to the action plan.
➢ *Antimigraine Agents*	*Paula Townsend, PharmD*	**<u>Antimigraine Agents</u>** Dr. Townsend announced that there is a new generic, zolmitriptan for Zomig. Zolmitriptan nasal spray is now approved for acute treatment of migraine at a 2.5 mg starting dose (previously 5 mg) with the maximum recommended single dose still being 5 mg. It is now available in 2.5 or 5 mg devices. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.

➢ *Analgesics, Narcotic long-acting*	*Paula Townsend, PharmD*	**Analgesics, Narcotic long-acting** Dr. Townsend announced one new product, Zohydro ER (hydrocodone ER capsule). It contains a black box warning for addiction, abuse, misuse, respiratory depression, accidental exposure, neonatal opioid withdrawal syndrome and for its interaction with alcohol. There is no abuse deterrent component of the formulation to prevent bypassing the slow release properties. There is also a new generic morphine ER capsule for Avinza. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy or effectiveness between the agents, but that there were safety differences. Specifically there was some concern about the safety of methadone if prescribers are not familiar with its pharmacokinetic properties. There was also concern with Zohydro ER. The committee recommended placing specific PA criteria on Zohydro ER and to look at methadone use and possible educational opportunities.
➢ *Analgesics, Narcotic short – acting*	*Paula Townsend, PharmD*	**Analgesics, Narcotic short-acting** Dr. Townsend announced a new product formulation in this class, Xartemis XR (oxycodone 7.5/325APAP). The DEA ruling of reassigning hydrocodone-containing combination products from Schedule III to Schedule II is not expected until later in 2014. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. The committee expressed concern over the increase in use of oxycodone IR following the reformulation of Oxycontin (oxycodone ER). The committee recommended that a DUR study be done to look at oxycodone IR utilization including indication, dosage and use with or lack of use with long-acting opioids. They suggested a daily quantity limit of 60 mg per day be implemented. They recommended that Xartemis be non-preferred.
➢ *Opiate Dependence Treatments*	*Paula Townsend, PharmD*	**Opiate Dependence Treatments** There is one new product in the class, Zubsolv (buprenorphine/naloxone), indicated for the maintenance treatment of opioid dependence. It was approved based on a bioavailability study using Suboxone as the reference. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.

➢ *Skeletal Muscle Relaxants*	*Paula Townsend, PharmD*	**Skeletal Muscle Relaxants** Dr. Townsend announced that there was no significant new clinical information. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Antiemetics,/Antivertigo Agents*	*Paula Townsend, PharmD*	**Antiemetics/Antivertigo Agents** Diclegis (doxylamine/pyridoxine) is an anticholinergic/antihistamine and vitamin B6 analog combination which is FDA approved for the treatment of nausea and vomiting in pregnant women not responding to conservative treatment. These drugs have been available as separate agents OTC at a slightly different dose and have for a long time been recommended by the American College of Obstetrics and Gynecology and the Association of Professors of Gynecology and Obstetrics. There is no comparative data available for Diclegis. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Ulcerative Colitis Agents*	*Paula Townsend, PharmD*	**Ulcerative Colitis Agents** Dr. Townsend reviewed a new product, Delzicol (mesalamine delayed-release). It is bioequivalent to Asacol and Asacol was used in clinical trials to support the product. It is a reformulation of Asacol, removing two excipients which have been found to be developmental and reproductive toxicants. Uceris (budesonide enteric-coated extended-release) is a new product approved in January of 2013, but was not federally rebateable at the last review. Dr. Townsend reviewed the clinical trials supporting its renewal. **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
➢ *Idaho Hereditary Angioedema Agents(HAE) Guidelines*	*Jane Gennrich, PharmD*	**Idaho Herieditary Angioedema Agents (HAE) Guidelines** Dr. Gennrich provided an overview of Idaho's current clinical guidelines for treatment and prevention of Heriditary Angioedema attacks.

➢ *Hereditary Angioedema Agents*	*Paula Townsend, PharmD*	**Hereditary Angioedema Agents** Dr. Townsend announced that this is a new drug class to be reviewed by this committee. She reviewed the information regarding the treatments and clinical information for each of the drugs in the class. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents. They recommended that Cinryze as the only prophylactic agent be designated as preferred. The committee also recommended continuing to require prior authorization using the current therapeutic criteria.
➢ *Immunosuppressives, Oral*	*Paula Townsend, PharmD*	**Immunosuppressives, Oral** There is a new product, Astagraf XL (tacrolimus XL). It is not interchangeable with IR tacrolimus products. Generic sirolimus for Rapamune and generic mycophenolic acid for Myfortic are now available. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness or safety between the agents.
➢ *Multiple Sclerosis Agents*	*Paula Townsend, PharmD*	**Multiple Sclerosis Agents** Copaxone (glatiramer acetate) is now available in a prefilled 40 mg syringe for administration three times weekly. Rebif Rebidose (interferon-β –1a) is now available as a prefilled auto injector. Tecdifidera (dimethyl fumarate) is a new drug indicated for treatment of patients with relapsing forms of multiple sclerosis. Dr. Townsend reviewed the information from two placebo controlled clinical trials of Tecfidera. There are no comparative studies available. She reviewed the safety information, which includes flushing, abdominal pain, diarrhea and nausea. There is a warning for lymphopenia. Mean lymphocyte counts decreased during the first year of therapy but then remained stable. **Committee Recommendations** The committee concluded that the evidence did not support differences in efficacy, effectiveness

		and safety between the agents. Tecfidera is possibly more effective than Gilenya. The committee recommended having at least one oral agent as preferred.
➢ *Other Committee Business*	*Tami Eide, PharmD*	**Other Committee Business** Our next P&T Committee meeting is scheduled for October 17, 2014. There is no other committee business. The meeting adjourned at 3:45 p.m.

Pharmacy and Therapeutics Committee
Public Comment
May 23, 2014

Committee
Okay, next on the agenda is the public comment. So today, it will be the medical practitioners first, and then no one signed up for private citizen comment, and then there was no preapproved pharmaceutical representative comments, so first is Dr. Herrold.

Tracy Young, NP
Good morning. I'm actually here to talk about two medications that I use in my practice. I'm a nurse practitioner, I'm sorry, Tracy Young, nurse practitioner from The Digestive Health Clinic. For the last, almost, ten years, I have been dealing with a great deal of liver disease in our area, as well as a lot of other gastrointestinal disorders. The two drugs that I would like to address today are Xifaxan (rifaxamin), which is an antibiotic which we use in combination with lactulose for recurrent encephalopathy for our patients with cirrhosis. It's a drug that I like very much, although I do not use often. Fortunately, most patients are pretty compliant with their lactulose dosing, but some of them cannot tolerate it, and those patients, probably two or three a month, end up in the hospital with recurrent encephalopathy. The only way that we have been able to control that is with the use of rifaximin in combination. Patients, themselves, appreciate almost immediate cognitive improvement with the use of rifaximin, and again I have had two patients just in the last six months, who have had repeated ICU stays that were very expensive, that the only way I kept them out of the hospital was with the use of Xifaxan. I know it's an expensive drug, but I think that appears to be fairly cost effective as opposed to ICU visits.

The other medication is sofosbuvir, Sovaldi.. This is the newest kid on the block in the treatment of hepatitis-C. It is a very potent agent. It's the second in a wave of new, direct-acting antivirals. Just to give you a little history of my perspective on the treatment of hepatitis-C, in May of 2011, when the first protease inhibitors were introduced, between May of 2011 and August of 2013, I treated 49 people with hepatitis-C. Thirty-nine of those were genotype-1 and required triple therapy using protease inhibitors. Unfortunately, eleven of those were discontinued because they did not have an adequate response, or they were intolerant to side effects. Sixty percent of the remaining achieved SVR, which is defined as "cure". More than a fifth of those required either erythropoietin or transfusions, as well as ribavirin dose reductions. So that was over a 27-month period. In the last 5.5 months, I have started 41 patients on treatment using sofosbuvir or Sovaldi. Of the 30 that have made it as far as four weeks into treatment, because the rest, again, have not made it that far, of those that have made it past four weeks, all of them either had an undetectable viral load at week-4, or detectable or unquantifiable, which I believes means you meet therapeutic criteria. Only one has required a transfusion. Several of them are only seen on a monthly basis, as opposed to previous therapy, where I saw them at least every two weeks. The lab draws have gone down significantly because anemia is very, very, very, much less of an issue. Again, only one transfusion, and that is in a patient with cirrhosis. Six of the patients I am currently treating have compensated cirrhosis, and two of them were completely no-responders to prior therapy. I have some concerns about your potential therapeutic criteria. On your criteria, you note "Patients will be excluded without documented evidence of successful completion of six months of abstinence for injection drug use and/or alcohol dependency." I am concerned about how you're going to define "alcohol dependency" and who is going to be monitoring that. The second is that, to my understanding, you're intending to exclude anyone who does not have stage-3 or stage-4 fibrosis, but since our biopsies, and although our pathologists and our radiologists are very good, our biopsies are vulnerable to sampling variability, and I have had a couple of patients with stage-2 on biopsy that, within two years, had cirrhosis, and I know they did not progress that fast; it was the variability of that sample. So I'm hoping that you will include stage-2 as well. The last is that you're asking for viral loads to be drawn at two and four weeks, and I'm not understanding why that is. The viral loads are an expensive test and I know that you're trying to save money, so the two and four weeks appears excessive. It really doesn't serve any purpose, because we don't change therapy. Thank you very much for listening.

Committee
I'm sorry, our criteria has not, we don't have criteria, if they're here for approval.

Tracy Young, NP
Potential. I'm sorry.

Committee

Okay, but we really haven't published those. Those aren't out there, so.

Tracy Young, NP
May I address how I know them? Dr. Ike Tanabe, one of my colleagues, was asked for his opinion about the potential therapy, and since I do hepatitis-C treatment, he asked what I thought, and so I gave him my input on that. I was just reiterating some of my biggest concerns with this. I apologize if I'm jumping the gun.

Committee
Okay, and then I had a question about the Xifaxan. When you put someone on it, do you continue the Lactulose?

Tracy Young, NP
Yes, absolutely. It's not meant to be used in monotherapy.

Committee
Okay, that was my question, because that is how it's indicated.

I've got one third one; How would you monitor this. Do you have any suggestions, um, for sobriety?

Tracy Young, NP
Well, my first question to you would be, because, again, this, your potential criteria, had said "Alcohol dependency" which, it's a very subjective term, I think. I, with patients' permission, because I don't do any hidden lab work on them, if I have questions, then I will do spot testing for drugs or alcohol, but I don't typically, for the most part, I trust my patients, I develop a relationship with them, as well as their support system, so then I am pretty familiar with that, and patients that I have a question, I say "I'll see you in six months, so tell me you're going to AA, tell me you have a sponsor" or whatever. That's how I have addressed it. But, again, you know, unless you're testing them repeatedly, which becomes cumbersome, and at that point, if we're not trusting them that much, I don't think they're going to be very adherent to therapy anyway.

Committee
Can I ask a quick question, which is, I totally understand what you're saying about the potential for sampling error in liver biopsy, um, how much can be made up for that by radiologic diagnosis?

Tracy Young, NP
An ultrasound or a CAT scan, because we don't have FibroScan. But an ultrasound or a CAT scan can identify cirrhosis. Other than that, not.

Committee
What of hypertension, um.

Tracy Young, NP
Well, they'd be cirrhotic at that point. So anything up to that, and my big concern is, "Do I have a stage-3 that I'm missing because they identified it as a stage-2?" and all of a sudden I have decompensation on my hands.

Committee
And are there evidence-based guidelines that include stage-2? Or is that just kind of a clinical approach right now?

Tracy Young, NP
Just the clinical approach.

Committee
Okay, thank you. Any other questions? Thank you.

Tracy Young, NP
Thank you very much. You know, I wanted to say, when you mentioned that your goal was to do the best medication for the best price, these are the best medications. Good luck with the best price.

Committee
Dr. Stephen Asher?

Stephen Asher, MD
Good morning. I'm Stephen Asher, I'm a neurologist. I have been in practice in Boise for a number of years, and thank you for these two minutes. I just wanted to speak about MS drugs and make a plea for open access to the array of products that we have. There certainly are some that I use more than others. The history of the introduction of these drugs, I think you're all familiar with, since the

interferons have been out since the early 90s. I should just back up and say I have, in the past, spoken on behalf of Serono, Novartis, and Teva. I'm speaking here on my own behalf and I'm not being paid to speak to you today. Anyway, so we have a number of interferon products that are out there, and I think they really do all have their niche. I think probably from the standpoint of the prescriptions that you see coming through, you probably have as good of an idea as anybody as to what is commonly prescribed by practicing neurologists here. I can talk more about that if you have specific questions. Copaxone has been out a number of years as well. It has been a daily drug since its inception. It has recently been reformulated as a double dose, three-times-a-week product, which I think is a worthwhile addition to what we have to offer. One of the problems with daily injections, I don't have to probably emphasize, is that people do become fatigued with their needles. Having the option of something three times a week, I think, is desirable. Efficacy is comparable. The interferons that are commonly used are either, at present, weekly or three times weekly, so if someone is, for example, switching from an interferon to Copaxone (glatiramer acetate), having it available three times a week would allow them to maintain a rhythm or a cycle of injections that they are used to receiving. A lot of people really do get tired of having to poke themselves every day. There are three oral drugs currently available. I personally use two of those three. They each have a distinct and special niche, in part because of potential for side effects, but also mechanisms and efficacy, but I would hope that at least these two, which have better efficacy compared to the third, would be made available to your clients.

And then lastly, Tysabri is a great drug. It is one that we often use for the most aggressive and difficult to manage situations with respect to multiple sclerosis, and I would hope that we could continue to have that made available to us. I'm done.

Committee
Which were the two oral drugs?

Stephen Asher, MD
Which were the two oral drugs? There's Tecfidera and Gilenya.

Committee
Okay, and the Tecfidera has a better safety profile in your opinion?

Stephen Asher, MD
I think the two orals that I've mentioned both have sound safety profiles. I think that each need to be monitored. I think there are some differences in side effects. I think efficacy, in my view, is very comparable, and it looks to me that the hazard of meta-analysis, but they look like they're probably more effective than the currently available injectables, except for Tysabri.

Committee
And in terms of the Copaxone 40 mg, which is commonly thought that cutaneous side effects [inaudible].

Stephen Asher, MD
Sure. So side effects, there is not a study in which one has been compared to the other, so we have to take data that was available when the daily drug was introduced versus the three-times-a-week drug. There is the potential and commonly we do see injection site reactions. The intensity of the reaction, I really couldn't comment on, but I think that since it is a larger dose of active compound of glatiramer acetate, my guess is that the cutaneous injection reaction will probably be slightly more with three times a week than with the daily. The other that we run into is cutaneous lipoatrophy at the injection sites, and I think, in so far as we can reduce the number of those injections, we will have less resistance to the continuation and the compliance with an effective therapy. So I don't know if that answers you, but that's probably the best I can do in the absence of direct comparative data.

Committee
Any other questions? Thank you very much. Dr. Jim Herrold?

James Herrold, MD
Hello, my name is Jim Herrold. I'm a neurologist here for about seventeen years, and I've been here before. So I came out to just speak on behalf of my MS patients. If you have MS today, and you come into my clinic and you have moderate MS, the best drug, in my opinion, is Tysabri. It's given once a month, it's intravenous, with the caveat that right now, we're checking JC virus antibodies every six months, and if you're positive, then you're at risk of getting PML. If you're negative, if I have MS, I want to be on Tysabri. It reduces MS relapses about 66%. If you're JC virus antibody is positive, then we need to follow you closely and usually most of us get a little skittish and take people off those drugs, but, it's a good time to have MS if you're going to have it now, because there are now two orals that I consider. I don't, without throwing sticks at any drug; Aubagio is category-X for pregnancy, and a lot of women have MS. We don't use that drug. The efficacy is not that great. It's not as good as Copaxone, Avonex and so forth, so when I think of the oral drugs, we're talking about Tecfidera that's given twice a day, it has some potential GI side effects, maybe up to 20% of people just don't tolerate it, so we give it with food or we give it with a fatty meal, and most people do okay. Then some people get flushing similar to niacin, and we can offset that by giving aspirin before the Tecfidera to get rid of the flushing, but it's a pretty well tolerated drug. It reduces relapses about 50%, so that would be a consideration for the second drug I would choose for myself. Gilenya is a very good drug. It has the stink of causing bradycardia, so patients that have any sort of dysrhythmia or cardiovascular history need to get a, everybody gets an EKG in advance, and if they're on any drug that would effect AV node pathway, or they're

prone to bradycardia, it kind of scares us away from that drug. It's a little bit difficult to administer, because the first, and the first dose only, needs to be monitored with heart rate and blood pressure. So for six hours, the patient sits and waits and gets monitored. After you get through that first day, though, with Gilenya, there's no long-term cardiac side effects. So a lot of patients need to be educated that there's not long-term cardiotoxicity with Gilenya, but you've just got to make it through that first monitoring. So the drugs, like Dr. Asher said, Gilenya and Tecfidera have a similar efficacy. Tecfidera probably has a little less dangerous profile, so I sort of prefer Tecfidera because of its ease of use and then Gilenya is the second consideration if they don't have any cardiac issues.

Then, finally, we get back to the good old standbys of the interferons and Copaxone and, as Dr. Asher said, Copaxone used to be a daily subcutaneous and now it's three times a week; less, you know, half as many shots, and coming in this fall, Avonex, which is now a weekly IM injection, is going to be every other week, so it'll be twice a month. So I still think we need to keep drugs like Copaxone, Avonex which is a low-dose interferon, and perhaps Rebif, which is a high-dose interferon, as platform therapy, but in my practice, when I have a new patient and I offer them the shot or a pill, most of them sign up for pills if they have an option. So I think Tecfidera is going to be a popular drug going forward. I'm not sure of the cost difference between those, so, yeah, that's essentially all I had to say. I'll be happy to answer any questions.

Committee
I have one question, and I don't know if you'll have data on this, or if this is just experiential, but this just occurred to me. In 2014, when an MS patient has exacerbation, you know, what percent of the time do they end up getting admitted, and how long of a process to recovery, rehab has it tended to be?

James Herrold, MD
You know, most patients do not get admitted. So you're talking about a major exacerbation. A lot of patients will have new onset of a little bit of weakness in their leg or some numbness or some visual symptoms, and often we can treat that outpatient through the ambulatory care center with IV Solu-Medrol for three days. That's more of the norm. I don't know a percentage, I would guess, maybe 10? 10% or 20% would get admitted to the hospital for treatment? Most of the time we can do it as an outpatient.

Committee
And generally those admissions are relatively brief?

James Herrold, MD

They're brief. They essentially come in, it's the same treatment, in fact, they get treated with IV Solu-Medrol. If there's a superimposed infection; pneumonia or UTI, that gets treated aggressively, and in terms of recovery, you know, the more severe the relapse, the longer the recovery, or you may have incomplete recovery, but the Solu-Medrol effectively gets the patient through their exacerbation quicker, but it has not been proven to alter their long-term prognosis, so some patients that don't tolerate steroids elect not to get steroids, because it's not going to affect how they end up long term.

Committee
Okay, thank you.

Now, you've said injections, is this leading to followup wound care, or is it just a nuisance that leads to lack of compliance and not wanting to continue.

James Herrold, MD
I didn't understand the first part of the question?

Committee
So, both of you had alluded to the injections on a daily basis being a nuisance, and site reactions (Copaxone). Is that leading to, like, followup wound care?

James Herrold, MD
No. I don't know. Copaxone has been around a decade plus. It's been around forever, so they get a little, some patients get a little inflammation around there. Occasionally, there's some fat atrophy, but for the most part, these patients can inject like a diabetic, in the thighs, the shoulders and the abdomen, and there's not a lot of infection.

Committee
So you don't experience many stopping therapy on that because of the nuisance of the injections.

James Herrold, MD
Um, well, if I gave you the choice of, in the past, like a daily injection of Copaxone or a once-a-week of Avonex, or a pill, or an infusion once a month, you know, in terms of, it's sort of intuitive that, diabetics are used to injecting and MS patients get used to injecting, but the nice thing with Copaxone is that it used to be daily, but now it's three times a week, and I think there's very similar

efficacy in the drug. But the interferons and Copaxone, they reduce relapses about 30%. The pills, Gilenya and Tecfidera, they reduce relapses about 50%, and Tysabri is about 66%, just in round terms. And then, we also know that certain patients are specifically, their immune systems are responsive to, say, Copaxone, and it statistically they may do better on Copaxone or Avonex than they would do on Tecfidera or Tysabri, so it's a little bit individualized, but, um, I would be opposed to making everybody go on platform therapy with Copaxone, Avonex and Rebif, and when they get whacked with an MS flare-up, then they graduate to a better drug. I think you get behind and people can get permanent neurological disability if you do kind of a stepwise approach of having to fail one of those drugs before you get allowed to be on Tysabri or Gilenya or Tecfidera.

Committee
So I was curious, especially with the oral agents, you know, most of these cases I am assuming that are remitting/relapsing type cases.

James Herrold, MD
85% of the cases are, yes.

Committee
So when they are not in the relapsing phase, are they taken off the oral medications or is this basically a lifelong, once they're initiated, they are on it continuously?

James Herrold, MD
It's a good question. Most patients, 85%, have relapsing/remitting, and then a large percentage of those, after many years, ten years-ish, will progress into what's called secondary progressive. There are no studies that show that there are any drugs that work for a secondary progressive, but we don't want to learn the hard way, and sometimes patients that you think are in secondary progressive, and then you take them off a drug and they'll relapse, and then it just takes a couple of patients like that to kind of learn the hard way. So as a general rule, when you get diagnosed with MS, you just stay on a therapy, except if patients are older, when I take a patient off, they're usually 60-70 years of age and their MRI scans have been quiet for years, and they haven't had any definite MS relapses, but they may have secondary progression, whether they come in and they say they're slowly getting worse with their gait and just nonspecific stuff, but it's kind of a tricky thing. You know, when do you sell your stock? You know, you don't know if it's going to go up or down, but it's kind of a lifelong therapy, and even, there are some people who may have kind of benign MS that you figure out after you follow for a while, but the dogma is, if you've got MS, you put them on a therapy to reduce your risk of a relapse and neurological disability. All right, thank you.

Committee
Thank you. So that is all of our public testimony. Thank you if you spoke to us.