

Douglas Fish: Welcome and apologies for the delay here as we troubleshoot some audio issues. We've had to go to plan B which is the microphone as a phone. So that's why it's a little scratchy. So, please bear with us. Hopefully it will suffice for the day. As Tony said, I'm Doug Fish. I am the Medical Director for the Office of Health Insurance Programs, otherwise known as Medicaid and the Board Chairperson and it's my privilege to call to order the July 14<sup>th</sup>, 2022 meeting of the Drug Utilization Review or DUR Board. I would like to welcome everyone who are participating in today's DUR meeting. We do have a big agenda which Tony Merola will review here in a few minutes. Just a few logistical items to mention; today's meeting is being broadcast over the Internet as usual. The webcast will be archived on the Department's website, posting of the archived webcast to the DOH website usually takes within 1 to 2 business days from the meeting. The archived webcast will also include the information that is displayed on the screen today. For those actively participating in today's meeting including our DUR Board members, our support staff, and public speakers, please remember to keep your microphones or audio device on mute until such time as you are providing comments or have questions, and that will help us minimize any background noise. We are a hybrid meeting today, so some of us here in the room including some of the DUR Board members so thank you, and some of you are virtual and we appreciate all your participation. So, at this time, I'll turn it over to Kimberly Leonard our Pharmacy Director in the Medicaid Program for introductions and opening comments.

Kimberly Leonard: Thank you Doug. Welcome everyone. As always, thank you to our members for your dedication and willingness to continue to provide their clinical expertise to establish and implement medical standards and criteria for Medicaid's Drug Utilization Review program. Given that we're still operating remotely and in this hybrid model, I think what I'm going to do today is I will call names, call a roll for the DUR Board members and at that time, I would ask that you unmute and introduce yourself. I think we are lucky today. One of our newer members has been able to attend in person. So, I think I'll first turn it to Brock Lape.

Brock Lape: Hi, everyone. Brock Lape from the local area here and so, I am happy to be here as an advocate.

Kimberly Leonard: Thank you Brock. Next, we have Dr. Ignacio.

Dr. Renante Ignacio: Good morning.

Kimberly Leonard: Good morning. Dr. Radix.

Dr. Asa Radix: Good morning, can you hear me?

Kimberly Leonard: Yes, we can thank you.

Dr. Asa Radix: (can't hear)

Kimberly Leonard: Thank you. Dr. Chiarella. Dr. Chiarella, we are not hearing you. Maybe perhaps you're muted? Oh, there we go.

Dr. Joseph Chiarella: (can't hear)

Kimberly Leonard: Okay great, we'll have Georgia who is here with us switch you over to a panelist, thank you. Tara Thomas?

Tara Thomas: (can't hear)

Kimberly Leonard: Yes, we can Tara, thank you. Donna Chiefari?

Donna Chiefari: (can't hear)

Kimberly Leonard: Good morning. Dr. Najib?

Dr. Jadwiga Najib: (can't hear).

Kimberly Leonard: Thank you, good morning. Dr. Eglowstein? Well, alright we'll go to the next Casey Quinn.

Casey Quinn: Good morning this is Casey. (Very clear)

Kimberly Leonard: Good morning, Casey. How about Jill Lavigne?

Jill Lavigne: Good morning, this is Jill. (Very clear).

Kimberly Leonard: Good morning, Jill. Pete Lopatka?

Peter Lopatka: Good morning, I'm here. (Very clear).

Kimberly Leonard: Good morning. And John Powell?

John Powell: Good morning, everybody, John Powell from Department of Financial Services. (Very clear).

Kimberly Leonard: Good morning, John. And I think we'll try again for Dr. Eglowstein? No, okay. Alright, I'm going to turn it over to Tony so Tony can do a walkthrough of the agenda.

Tony Merola: Sure Kim, why don't we just do introductions for us around the table here. So, I'll go first and then we'll just go around. I'm Tony Merola, I'm a pharmacist with DOH.

Kim Laurenzo: Kim Laurenzo, Pharmacist Department of Health.

Barb Rogler: Barb Rogler, University of Buffalo.

Monica Toohey: Monica Toohey, New York State Department of Health.

Kim Leonard: And then Tony how about we turn it over to Buffalo and have them introduce.

Tony Merola: Sure, that's great, those in Buffalo could you introduce yourselves?

Linda Catanzaro: I am Linda Catanzaro.

Tzu-Yin Kuo: Hello, my name is Tzu-Yin Kuo.

Debra Targoff: Debra Targoff, University of Buffalo.

Irene Riley: Irene Riley, University of Buffalo.

Edward Bednarczyk: Ed Bednarczyk, University of Buffalo.

Holly Coe: Hi, Holly Coe UB.

Kim Leonard: Okay, thank you. And I just want to recognize Dr. Eglowstein is on but she's having some connectivity issues due to some storms in her area so.

Tony Merola: So, in addition to Marla Eglowstein, Deb Wittman is also on the line, one of our other DUR Board Members.

Deb Wittman: Good morning, everybody. I'm Debra I'm with Mount Sinai in the Department of Medicine also Pharm D and we're based in New York City.

Tony Merola: Thanks Deb. Okay, let's jump right in. I just have a quick roadmap of what we have on the agenda. So, the first agenda item is pharmacy program update. Kim Laurenzo will be doing that for us and it's an overview of a new initiative. The Management of Physician Administered or Practitioner Administered drugs or the longer description of that is establishing parity or uniform clinical standards or clinical criteria for drugs covered across the pharmacy and medical benefits. This overview will play into those DUR review items on the lower part of the agenda. After that update, we'll move into the Preferred Drug Program, there are 5 drug classes that we will be reviewing today; 3 have new clinical information since the previous review, those would be the antipsychotics- injectable, antipsychotics- second generation, and immunomodulators- systemic. So, there's new clinical information since the previous review for those three classes. Other agents for Attention Deficit Hyperactivity Activity Disorder, we have new financial information there and then a new class that we're calling our Glucagon Agent. So those are the five classes. All five classes will be reviewed when we recess to Executive Session and then as I mentioned, there's three drug utilization reviews: Aducanumab, botulinum toxins, Infliximab and Vedolizumab. So, those are the DUR items that we hope to get to this afternoon. So, without further ado, I think we'll jump right into the public comment period. So, at this time, I will ask Georgia to pull up the speaker list. So, this is the order for which the speakers will present. We are going to ask the speakers that are here in person to use that podium. But give me a minute, I'm going to transition to that podium because I want to make sure the microphone works. Okay, I think the microphone works. So, while I give the instructions why don't I call Tim Birner up because he's got the first two speaker slots. Tim, just stand here just for a minute and let me give some instructions, then we'll get started.

So, at this time we'll have the speakers present their testimony. Public comments are limited to specific topics on the agenda and must be no longer than 2 minutes. Just keep in mind that your testimony has already been provided to the DUR Board, so we find that if you're running a little shy on time, just to summarize your comments. But again, public testimony has already been provided to the DUR Board before this meeting. So, the process, so before jumping into your

comments, I would ask that you introduce yourself, who you represent, and whether you have any financial relationships or conflicts of interest related to today's meeting and then we will start the clock per se. You don't have to abruptly stop, but we do ask that you consider that 2 minutes and if you find yourself short of time, we would ask you to conclude. So, here's the speaker list, it looks like Tim has the first two speaker slots. So, Tim, I will turn the microphone over to you.

Tim Birner: Well, good morning. My name is Timothy Birner, I'm a PharmD UB grad, Senior Director of Medical Affairs at Alkermes, so I'm an employee of Pharma, and thank you for the opportunity to provide testimony on Aristada, which is Aripiprazole lauroxil, an extended-release injectable antipsychotic. Aristada is indicated for the treatment of schizophrenia. The efficacy of Aristada is in part based on a 12-week randomized double blind placebo-controlled registration study. The primary efficacy variable was the change from baseline to endpoint and PAN total score. In a statistically significant separation from placebo was observed on the PAN total score for each Aristada dose. The most common adverse events were insomnia, akathisia, and headaches with akathisia being the most commonly observed adverse reaction with Aristada. Aristada does have a black box warning which is a class warning for increased mortality in elderly patients with dementia related psychosis. Depending on an individual's patient's needs, treatment with Aristada can be initiated at a dose of 441, 662 or 882 mg administered monthly, or the 1064 mg administered every 2 months, which corresponds to 300, 450, 600 mg and 724 mg of Aripiprazole respectively. Treatment may be also initiated with 882 dose every 6 weeks. Aristada initio which is a newer agent in combination with oral Aripiprazole is indicated for the initiation of Aristada when used for the treatment of schizophrenia. Aristada initio is part of a one-day initiation regimen along with a single 30 mg Aripiprazole dose given in conjunction with the first dose of Aristada. The one-day initiation is an alternative to twenty-on days of oral Aripiprazole prescribed at the first dose of Aristada. The main formulation different between Aristada and initio is the particle size of the crystals. To summarize, Aristada and initio is part of a one-day initiation along with a 30 mg tablet give in conjunction with the first dose of Aristada and is an alternative to twenty-one days of oral Aripiprazole. Aristada is the first long-acting atypical antipsychotic with both once monthly, six week, and every two months for dosing. These results support Aripiprazole or Aristada as an important treatment option. We ask that Aristada be continued to be preferred in the PDL and at parity with the other long-acting injectables. Thank you.

Tony Merola: Thank Tim. Any questions for Tim on Aristada before he moves onto his next topic?

Tim Birner: I will now thank you for the opportunity to provide testimony on Lybalvi. Although efficacious with the treatment of schizophrenia and bipolar 1 disorder, Olanzapine has been associated with a risk of significant weight gain. Lybalvi is a combination of Olanzapine and samidorphan which is an opioid receptor antagonist. It is indicated for the treatment of schizophrenia and bipolar 1 disorder in adults. The approval of Lybalvi in schizophrenia is

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partially based upon adequate and well controlled studies of orally administered Olanzapine and on 2 phase 3 randomized clinical studies of Lybalvi. In enlighten 1, Lybalvi demonstrated statistically significant improvement in the PAN score compared to placebo at 4 weeks. The inclusion of samidorphan and Lybalvi did not appear to negatively impact the antipsychotic efficacy of Olanzapine. In enlighten 2, Lybalvi met its coprimary endpoints demonstrating significantly less weight gain from baseline at week 24, and a significantly lower proportion of patients who gained more than 10% of their body weight compared to Olanzapine at week 24. Lybalvi patients were half as likely to gain 10% of their baseline body weight over 24 weeks compared to patients treated with Olanzapine. Lybalvi's most common adverse events in schizophrenia were increased weight, somnolence, dry mouth, and headache. Lybalvi has a boxed warning for increased mortality in elderly patients with dementia related psychosis. Samidorphan is an opioid antagonist and can precipitate opioid withdrawal. Lybalvi is contraindicated in patients taking opioids or undergoing acute opioid withdrawal. An opioid free interval is therefore required prior to initiation. In closing, Lybalvi illustrated significant less weight than Olanzapine while providing the same antipsychotic efficacy in adult patients with schizophrenia. We respectfully ask that Lybalvi, and we're fully comfortable with it not being on the PDL, we fully expect patients are going to use a couple of generics before they go to a branded agent, but we ask that it be at parity with the other branded antipsychotics. So, thank you for your time, and I would be happy to answer any questions.

Tony Merola: Any questions for Timothy?

Female: Yes, can I ask a question please?

Tony Merola: Sure, and this is Jadwiga?

Jadwiga Najib: Yes, this is Jadwiga. I have a cold so if my voice sounds scratched, it was noted that the combination had significant decreases in weight gain and smaller increase in waist circumference, however there was no real significant differences for fasting glucose, nonfasting hemoglobin A1C and cholesterol total, HDL, LDL, triglycerides. So, do you have any recent data on this and also, the study looks at BMI between 18 and 30, we have a lot of patients that fall outside that BMI range, any data that you have from the company on those patients outside of that BMI? And any comparative data with Metformin that might be used for that kind of condition? And also, what happens if the patient has a dose that is going to be higher than the recommended dose? Because the dose of the weight loss agent is 10 mg I believe for each of the doses of the Olanzapine and so is there any data that higher doses might be more problematic or any concerns with that. Thank you.

Tim Birner: Yeah, thank you for those thoughtful questions. To your first question, we have this enlightened 2 study that lasted head-to-head study against Olanzapine that lasted for 6 months. There was really no difference in the metabolic parameters at that point, but when we had a one-year extension. So, now these patients are all converted to Lybalvi, so now we're a year and a half out, and what we noted was there were no increases in those metabolic parameters nor was

there any additional weight gain. So, I just want to mention, Lybalvi is not a weight loss drug, it's not a drug for diabetes, the whole intention is not to cause some of these comorbidities. Now, there are some limitations because it was open label, it was an extension, there was no active comparator but in our extension data, we show no additional increases in LDL, cholesterol, weight, or A1C. regarding the strengths, it's available with a standard 10 mg dose of samidorphan. It comes in 5, 10, 15, and 20. If the physician wanted to use a higher dose of Olanzapine that would be off label. Lybalvi is only available in 4 commercial strengths. So, you can't take 2 Lybalvi because that would be off label and it would be too much samidorphan. But I do recognize that some patients are on higher doses of Olanzapine but we really our package label does not address that. There were a couple other questions.

Tony Merola: Metformin data.

Tim Birner: Metformin data. Well, you know Metformin, of course, is a drug for diabetes, it would be off label. We do not have any head-to-head data against, but we do realize that some psychiatrists do use Olanzapine in combination with Metformin, which again, is off label. We are on label.

Tony Merola: And the BMI between 18 and 30.

Tim Birner: The reason we limited the BMI to 18 to 30 we thought it would be unethical to exposure patients with a BMI greater than 30, morbidly obese to olanzapine. So, we just felt we couldn't include patients that were morbidly obese, but yes, our study limited it to patients between a BMI of 18 and 30 at onset. But that was the rationale. Thank you so much, those are great questions.

Tony Merola: Any other questions for Tim?

Tim Birner: Thank you for reminding me what the questions were.

Tony Merola: Thanks Tim. Next speaker Kimberly Blair. Kim, can you unmute your microphone?

Kimberly Blair: Hello everyone, can you hear me?

Tony Merola: Loud and clear, thanks Kim.

Kimberly Blair: Love it, thank you so much for having me today. So, my name is Kimberly Blair and I'm testifying at the Director of Public Policy and Advocacy for the National Alliance on Mental Illness in New York City, or NAMI NYC. We don't have any financial interest or conflicts of interest. So, I am honestly here today as a peer with experience as well as to support a family member of someone else living with schizoaffective disorder. I am here because we our NAMI NYC members know all too well that getting the right medication regimen can be a long and challenging process, but getting the right medication is often what makes a difference between a disability and stability. New advances in medication and their combination with other services support and allow individuals with mental illness to lead healthy and productive lives.

We would like to see an increase in access and accessibility to antipsychotics including long-acting injectable medication. Important, we see antipsychotic and antidepressant medications as not interchangeable as most of you know since a lot of you have PharmD next to your names and provides must be the ones to be able to select the most appropriate and clinically indicated medication for their patients. So, while psychiatric medications may have similar effects overall, they are unique in their mechanisms of action and affect each person and range of symptoms, differently. Patients respond differently to antidepressant and antipsychotic medications, and it often require multiple trials and many months to find an appropriate drug regimen that stabilizes an individual's condition. Specifically, during this pandemic, my own family member has had a number of issues accessing medications due to closures of the one community health clinic at the beginning of the pandemic where she was accessing her medications. This story is not unique. There are many barriers to being able to access medications, and we really need access to a full spectrum of psychiatric medications because it's a critical component of community-based care. So, we have advances in medication and other services over the past few decades that have enabled care and treatment of SMI to take place in a large part in the community leading to a decreased reliance on inpatient facilities. Ability to access long-acting injectable medications in any pharmacy or community-based setting, makes community-based care more effective as it leads to increased compliance with medicine regimen and better long-term recovery outcomes. we know that there is state legislation that has been working to increase access, but even so, when they go through all the amendments, it still is minimizing access for our NAMI NYC members especially those who have dual diagnoses, so they have co-occurring substance abuse disorder and maybe a serious mental illness. Individuals with medical health conditions were unable to access the most appropriate clinically indicated psychiatric medication experienced higher rates of emergency department visits, hospitalizations, and utilization of other health services. So, policies that restrict access to medications have shown in a variety of published studies to cause increase in hospitalizations, lengthier hospital stays, more ER visits, more outpatient hospital visits, and we already know right now that there are not enough beds, especially those that have not been returned from the COVID-19 State of Emergency. A study by Joyce West in General Hospital Psychiatry analyzed Medicaid data from 10 states and found that psychiatric patients who reported access problems with their medications visited the ER 74% more often than those who had no difficulties accessing their medication. Rates of suicidal behavior and homelessness also rise among patients who report difficulties accessing their needed medications. In my own experience with my family member, lack of access to her long-acting injectable medication and other medications nearby in her nearby pharmacies or community-based settings have often caused with issues with her NYSA housing, maybe she is having episodes that she wouldn't have otherwise had if she was on her medication and had regular access to it.

Tony Merola: Kim, sorry to interrupt but we would ask you to conclude.

Kim Blair: Oh, yes, of course. So, in conclusion we submitted the written testimony and I hope you do take this into consideration.

Tony Merola: Thank you Kimberly. Any questions for Kim? Okay hearing none, the next speaker Ameen Saleem and while Ameen unmutes himself, I would probably ask Arden Arslanyan is here, I'd ask him to just come to the mic so we can transition smoothly there. So, Ameen Saleem.

Ameen Saleem: Good morning, just checking you can hear me.

Tony Merola: Loud and clear.

Ameen Saleem: Thank you. Good morning, my name is Ameen I'm a medical liaison represent Intra-Cellular Therapies. Thank you for the opportunity to speak today about Lumateperone brand name Caplyta an atypical antipsychotic indicated for the treatment of schizophrenia as well as depressive episodes associated with Bipolar 1 and Bipolar 2 disorder as both monotherapy and as adjunctive therapy with Lithium or Valproate. Caplyta approval for the treatment of Bipolar depression in adults was based on two positive randomized double-blind placebo-controlled study. In both 6 weeks, monotherapy, and adjunctive therapy studies Caplyta 42 mg for 6 weeks specifically separated from placebo on the primary efficacy of the outcome of the Madras total score and also on the key secondary outcome based on clinical rated scale the CGIPS score. The most common adverse reactions to Caplyta 42 mg in both short-term study at a rate of greater than 5% and twice the rate of placebo with somnolence, sedation, dizziness, nausea, and dry mouth. Mean changes from baseline in metabolic parameters including fasting glucose, insulin, total cholesterol, and triglycerides as well as body weight and prolactin levels were similar to placebo. Motor effects were also \_\_\_\_\_. There were no single treatment emergent adverse events that led to discontinuation in greater than 2% of patients. The emergence of mania and hypermania in both acute studies were similar to placebo. In a 6-month open label trial of Caplyta in patients with Bipolar depression, the proportion of patients with a shift to normal to high were 10%, 5% and 2%, the total cholesterol, triglycerides, and LDL cholesterol respectively. The main change in body weight was -0.01 kilograms with a clinically significant weight increase or decrease in 4.8% and 5.6% of patients respectively. Multiplied effects such as esthesia and akathisia were 2.4% and 1.6% respectively. No new safety signals were observed in the longer-term treatment and efficacy was maintained at the end of 6 months. And again, I'll refer to the prescribing information for any precautions or warnings and is also available there. And I thank you for your time and consideration.

Tony Merola: Thanks Ameen. Any questions? Okay and standing at the podium and ready to present next is Arden Arslanyan.

Arden Arslanyan: I'll take it. That's okay. So, my name is Arden Arslanyan and I'm here representing Otsuka Pharmaceuticals. I just wanted to thank you for the opportunity here to present Rexulti and I believe you have already received the full prescribing information as well as this testimony, but I just want to take a few minutes to highlight some clinical points. So, regarding major depressive disorder, monotherapy antidepressants were widely recommended as first line treatment to MDD and although multiple monotherapy antidepressant treatments are



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available in various therapeutic classes, approximately 50% of patients with MDD do not achieve response to initial monotherapy. Antidepressant medications one-third do not achieve remission after multipole treatment trials. So, regarding indications and usage, Rexulti chemical name brexpiprazole, this is an atypical antipsychotic. It is indicated for the use of adjunctive therapy to antidepressants for the treatment of MDD in adults, as well as the treatment of schizophrenia in adults and pediatric patients ages 13 years and older. Regarding real world studies, improving patient life engagement and functioning are important goals in treating MDD. Efficacy and safety of brexpiprazole, they have been demonstrated in phase 3 randomized controlled trials. A post hoc analysis of trial data showed improvement in life engagement following initiation of adjunctive brexpiprazole in patients with MDD. A retrospective real-world study evaluated 624 patients, adults, diagnosed with MDD and prescribed brexpiprazole for at least 30 days between 2014 and 2020 from greater than 25 hospital care systems. Statistically significant changes in life engagement scores were observed from as early as one month after the index events, which was the first prescription. Within the first six months, 44.5% of patients demonstrated significant improvement in emotional domain as well as 45.6% patients demonstrated significant improvement in social domain. More than 50% of patients on brexpiprazole demonstrated an improvement in life engagement within 6 months with significant improvement being observed from as early as one month from initiation. In fair balance, I'll call your attention to the class white box warning for Rexulti, this is increased mortality in elderly patients with dementia related psychosis and suicidal thoughts and behavior in children and adolescents, young adults. So, in closing Rexulti is indicated for the adjunctive treatment of MDD in adults as well as the treatment of schizophrenia for adults and pediatric patients age 13 and older. We respectfully request that Rexulti, at the very least continue to remain available to patients in New York with the same access that they have received to date. I understand there's multiple components that go into making formulary decisions, but the patients are unique, the brain is unique. There is a reason Medicare has made this class protected. There is a reason why states are adopting legislation regarding Medicaid to improve access, and we ask you to consider improving access and not creating barriers to access. Thank you.

Tony Merola: Any questions for Arden? Seeing none, thank you very much. Next speaker would be Steven Burch. Do we have a good audio connection?

Steven Burch: Yes, can you hear me?

Tony Merola: Yes, loud and clear. Thank you.

Steven Burch: Great. Well, thank you, everybody. Glad to be with you this morning virtually. My name is Steven Burch and I'm the Director of Health Economics and Outcomes Research with Sunovion. Thank you for the opportunity to provide information in support of retaining Latuda in a preferred position on the PDL. I just have a couple of updates and won't take the full two minutes. Latuda or lurasidone HCL is indicated for the treatment of schizophrenia and adult Bipolar depression in adults and adolescents. Several Latuda studies have been published since the last review, and I refer you to the written testimony that I've submitted early. It provides a

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short summary of the network meta-analysis, post \_\_\_\_\_ analysis and retrospective comparative studies. It also gives the link, most of those are available online. Lastly, and what I believe the Board may be most interested to know is that Latuda will lose patent exclusivity in February of 2023. So, just a few short months away. So, given the short patent exclusivity period, Latuda addresses the need for well tolerated and cost-effective agent for both adults and adolescents with schizophrenia and bipolar depression, I respectfully request that Latuda be retained as a preferred agent on the PDL. Thank you for your time.

Tony Merola: Thanks Steve. Any questions for Steve on Latuda? Okay hearing none, Nirali Patel has the next three speaker slots on three separate products. So, we will take one by one, go ahead Nirali.

Nirali Patel: Sounds good, thank you Tony. Good morning everyone, can everybody hear me okay? My name is Nirali, I'm a medical outcomes and science liaison and I want to start today by thanking you for providing me the opportunity on behalf of Abbvie to showcase the clinical value of three of our products. The first one that I'm going to be talking about today is Vraylar which is a second-generation atypical antipsychotic, and then we'll move onto the two systemic immunomodulators Rinvoq and Skyrizi. Vraylar is an oral medication taken once daily approved for the treatment of schizophrenia and a full spectrum of treatment for Bipolar 1 disorder. So, this is inclusive of acute manic mixed episodes, as well as depressive episodes. Vraylar has established a safety and efficacy in more than 9 clinical trials across its indications. The most common adverse effects in these trials with akathisia and EPS. However, the discontinuation rates due to these side effects were less than 2%. There is a box warning regarding suicidal ideation and increased mortality in elderly patients with dementia related psychosis, and other warnings. I encourage you to look at the full prescribing information. Today, I will provide you with the three key differentiators of Vraylar compared to the other products that are in the market. The first is its unique mechanism of action. It is the only D3 preferring atypical antipsychotic medicine on the market, which in theory has benefits on the difficult to treat negative symptoms for schizophrenia. The second is that it has two active drug metabolites giving Vraylar the longest half-life compared to the other products. This is beneficial for patients that are intermittent adherent, especially because 80 to 90% of the patient with schizophrenia and Bipolar relapse after discontinuation resulting in increased costs. And finally, Vraylar has a neutral metabolic profile with a low risk of waking and sedation, extremely important because patients with Bipolar and schizophrenia are at an increased risk of early mortality due to cardiovascular disease. And finally, weight gain is a common reason for discontinuation of the medication. So, I have concluded. Are there any questions regarding Vraylar before I switch over to Rinvoq?

Tony Merola: Any questions in Vraylar? Hearing none, we can go onto the next topic.

Nirali Patel: Awesome. So, next we are going to be talking about Rinvoq also known as Upadacitinib which is an oral product indicated for rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, atopic dermatitis as well as ulcerative colitis. For the room and the UC

indications Upadacitinib is indicated for patients with a failure or intolerance to TNF blockers and for atopic dermatitis were approved for moderate to severe patients that have failed systemic therapies inclusive of biologics. I want to highlight three key attributes of Rinvoq across all of these indications. First, is its rapid enduring response. Second, its meaningful improvements in outcomes that patients and providers value. And third, is its favorable risk vs. benefits profile. Flaring of symptoms associated with UC contributes to increased costs, morbidity, as well as mortality. Therefore, patients and providers are constantly looking for options with rapid and lasting remission. So, recent update to the AJA guidelines now recommends that patients with moderate to severe disease should be put on biologic therapy soon after diagnosis with a target of achieving endoscopic remission because it can result in better long-term disease outcomes. In the UC trials, patients induced with 45 mg once daily for 8 weeks met the primary endpoint of clinical remission. And similarly, clinical remission was achieved also in patients that received 15 or 30 mg of Upadacitinib during maintenance. The unrelenting itch can be debilitating not only physically but also mentally for patients with atopic dermatitis. In addition, we are in need of agents that can lessen inflammation, redness, as well as thickening of the skin, all which increase the elevation of healthcare resources. In the three pivotal trials, Upadacitinib met all primary and key secondary endpoints. Approximately two-thirds of the patients achieved 75% improvement in their skin symptoms by 16 weeks and significant improvement in itch was seen just after 2 doses of Upadacitinib compared to placebo. Recent data released from a study of another JAK inhibitor vs. TNF blockers in a high-risk RA patient population showed increased rates of malignancies, BPE and all cause mortality with that JAK inhibitor. Upadacitinib safety is well studied with now having exposure in over 9,900 patients since 2012 across all of the indications. The overall safety is consistent across these indications, and we will continue to monitor long-term safety and efficacy. Again, I would encourage you to look at the prescribing information to get more details on safety. I'll stop here to see if anyone has any questions before I proceed to Skyrizi.

Tony Merola: Any questions on Rinvoq? Okay, hearing or seeing none, onto Skyrizi.

Nirali Patel: Thank you. So, finally I want to provide you an update on the two most recent indications for Skyrizi which are Crohn's Disease and psoriatic arthritis. The three words that sum up a patient's journey that lives with Crohn's Disease are unpredictable, overwhelming, and exhausting. Most say the disease controls their lives, not knowing how they will feel from one day to the next. As a new option in the treatment paradigm, Skyrizi can help patients that struggle to get to remission and stay in remission. Skyrizi is an interleukin 23 inhibitor approved for patients with moderate to severe disease. Patients would be given three IV doses as induction four weeks apart, and then continue maintenance given as a subQ injection using an on-body injector. The drug has contraindications in patients with previous hypersensitivity reaction to Skyrizi and its excipients and it is recommended to check liver enzymes as well as bilirubin prior to starting Skyrizi and during induction and then routinely thereafter. Similar to the updates in UC, AGA recommends moderate to severe patients with Crohn's Disease to be started on biologics soon after diagnosis. For these patients, time is gut. So, the sooner they are put on

appropriate therapy, the better chances of modifying the nature course of their disease. In the clinical trials for Skyrizi, both primary endpoints of clinical remission, as well as endoscopic response were achieved in biologic medications as well as biologic experiences. Skyrizi is also approved for psoriatic arthritis. In the two pivotal studies, Skyrizi met the primary endpoint of ACR20, as well as clinically meaningful secondary endpoint such as PASI which measures the ability to lower disability bargains and the higher bar end point of minimal disease activity compared to placebo. Safety in both psoriatic arthritis and Crohn's disease clinical trials is consistent with what we have seen in our psoriasis studies with now new signals to report. Please look at the full prescribing information to get more information regarding the safety. I want to close today by asking the Board to consider adding all approved indications for all three of these products to the State's PDL. Thank you so much for your time and I can take any questions you may have for Skyrizi.

Tony Merola: Any questions for Nirali? Okay, seeing none, thank you very much. Next speaker is Daniel Shan. Dan, do we have a good audio connection?

Daniel Shan: Hi, this is Daniel can you hear me?

Tony Merola: Yes, very well thank you.

Daniel Shan: Good morning, I'm Daniel Shan from the Medical Outcome Liaison with UCB. Thank you very much for letting me provide update on Certolizumab Pegol brand name Cimzia. Cimzia has a unique molecule structure and antibody without a fragment crystallizable region. Cimzia is the first and only approved anti TNF agent for the treatment of adults with non-radiographic exterior spondylarthritis nr-axSpA with objective signs of inflammation. Nr-axSpA is the painful and debilitating condition affecting the sacroiliac joint and spine, the burden of disease is similar to ankylosing spondylitis. In October of last year, nr-axSpA received its own ICD-10 code so it's no longer needed to be indexed to other conditions or category. Besides nr-axSpA, Cimzia is also approved for treating adult patients with moderate to severe Crohn's disease, moderate to severe atopic rheumatoid arthritis, atypical psoriatic arthritis, and ankylosing spondylitis, and moderate to severe plaque psoriasis. I want to highlight that there were some prospective probable kinetic trials of Cimzia in women of childbearing age, they demonstrated negligible to low percent of transfer and minimal transfer. The information is included in the full describing information. Those studies were designed only to assess transfer of drug from mother to infant. So, conclusions regarding Cimzia's safety and efficacy in pregnancy and nursing should not be made based on this data. Cimzia is available as prefilled syringe for self-injection, and a lyophilized powder for healthcare provider administration. Cimzia has a box warning in the PI. Serious and sometimes fatal side effects have been reported with Cimzia including sepsis and other serious infections. I would like to refer you to Cimzia's prescribing information for both safety and efficacy profile. Here I would like to respectfully request the committee to let Cimzia remain on the PDF so it can be an option for patients who can benefit from it. Thank you very much for your time.

Tony Merola: Thank you, any questions for Daniel? Hearing none, it looks like the next speaker is Richard Kraft.

Richard Kraft: Good morning, can you hear me?

Tony Merola: Loud and clear, thanks, Rick.

Richard Kraft: Excellent, good morning again, my name is Rick Kraft with Medical Affairs representing AstraZeneca and I do thank you for the opportunity to present information on benralizumab brand name Fasenra injection for subcutaneous use. The information I will discuss today is recent data on Fasenra per the PNT committee's request. Fasenra is a humanized monoclonal antibody that uniquely directly binds the alpha subunit of the IL5 receptor and reduces eosinophils through antibody dependent cell media toxicity. It's indication, dosage and storage remain the same as previously reviewed, highlighted by unique every 8-week maintenance dosing. For this testimony, again, we are focusing on recent data. Fasenra pivotal trials as well as Andhi and Ponente studies are detailed in the written testimony. The first safety study is Bora to discuss is a 68 week follow up in adults, 128 week follow up in adolescents, randomized double blind, long-term safety, and efficacy study of the Sirocco, Calima, and Zonda studies. The primary endpoint was safety and tolerability. And the full analysis set 1,576 patients included all patients from the Sirocco and Calima predecessor studies who received at least one dose of the study treatment in Bora and did not continue into the Meltemi study, a separate open label safety extension study. The safety and tolerability study of Fasenra was similar to that observed in the predecessor studies with no increase in frequency of overall adverse events. Next, improvements in exacerbations, lung functions, and eosinophils were sustained with benralizumab in the Bora study. For patients with blood eos of 300 or more who received Fasenra every 8 weeks continuously, 74% were free of exacerbations during the second year of treatment. Next up is Meltemi, this was 446 patients in an open label safety extension study for patients who had continued into the Bora extension study. For the integrated period, the benralizumab every 8-week group, at least 75% of patients had zero exacerbations per year for up to 5 years. Fasenra was well tolerated with a long-term safety profile consistent with the predecessor phase 3 severe asthma studies. Lastly, discussing some real-world evidence in asthma, the Zephyr 1 program was a retrospective cohort study of patients 12 and up with asthma in a real world setting taking Fasenra to identify the impact on exacerbations. In the primary cohort, those that had two or more records of benralizumab, the annual exacerbation rate demonstrated a significant 55% reduction and notably 41% were exacerbation free. In the persistence group, those defined as patients with 6 or more records in the 12-month post index period, the AER decreased again significantly 62%. Notably here, the Medicaid patients experienced a significant 49% reduction in the rate of asthma exacerbations and the non-Medicaid group also experienced significant reduction with 60% in the rate of asthma attack exacerbations in the post index period vs. the pre-index period. Medicaid patients did have higher exacerbation rates in both the pre index and post index periods vs. non-Medicaid patients. In closing, just a quick reminder that the first three doses of Fasenra are every 4 weeks and then

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the unique dosing of every 8 weeks subcutaneously thereafter for maintenance therapy. We are asking for continued coverage on the PDL, and we do thank you for the time and respectfully ask if there are any questions. Thank you.

Tony Merola: Any questions for Rick? Hearing none, thank you Ted Riley for stepping up to the mic.

Ted Riley: Absolutely. Thank you so much for the opportunity to come in today to be able to speak to the Board with regard to Nucala or mepolizumab. My name is Ted Riley, I am a National Field Medical Account lead with GlaxoSmithKline. Nucala mepolizumab is a subcutaneous injection targeted anti interleukin 5 monoclonal antibody for 4 eosinophilic disorders. The first being, it's an add-on maintenance treatment for adult and pediatric patients ages 6 and over with severe eosinophilic asthma. An add-on maintenance treatment for adult patients 18 and over with chronic rhinosinusitis with nasal polyps. There are going to be a lot of big words. Treatment of adult patients with eosinophilic granulomatosis with polyangiitis or EGPA and finally, for the treatment of adult and pediatric patients aged 12 and over who have hyper eosinophilic syndrome for greater than 6 months without an identifiable nonhematologic secondary cause. Limitations of use in Nucala is not indicated for either status asthmaticus or acute bronchospasm. Most common adverse effects, if we take a look at asthma, EGPA and HES, those occurring with an incident of greater than 5% are going to be headache, injection site reaction, back pain and fatigue. For nasal polyps, it's going to be oropharyngeal pain and arthralgia. So Nucala has a longstanding history of not only safety but improved patient outcomes in clinical trials and real-world data as provided in the data submitted to the Board. I wanted to take the opportunity to discuss two updates since that last time Nucala was reviewed. In the SEA space or severe eosinophilic asthma, reality A is an ongoing 2-year perspective observational study evaluating the effectiveness and safety of Nucala in a real-world setting. So, it's global. 12-month interim analysis has been completed and in this we saw that there was a 71% reduction in clinically significant exacerbations. This is within 822 patients, saw a 76% reduction in exacerbations leading to either hospitalization or ED visit, and from a select secondary endpoint, we saw that there was a baseline maintenance oral corticosteroid dose decrease from 10 mg at baseline to 2.5 mg at the 12-month interim analysis. Additionally, 43% of the patients were able to completely discontinue their OCS doses in the interim analysis. And then, since the last time the review was done, we have a new indication which is that chronic rhinosinusitis with nasal polyps. In our phase 3 synapse trial, we compared Nucala with placebo and standard of care in both arms. Standard of care typically being inhaled nasal steroids. Coprimary analysis was statistically significant improvements in nasal polyp endoscopic score as well as nasal obstruction visual analog scale that was done that was a patient reported outcome. And then select secondary endpoints, we saw 57% reduction in time to second nasal surgery, as well as improvements in quality of life as determined by the SNOT 22 scale. I would like to respectfully request that Nucala remain on the New York State PDL in a preferred position, and just wanted to thank you for your time, and see if anybody had any questions.

Tony Merola: Any questions for Ted? Hearing none, thanks. Next speaker Aaron Waltzer.

Aaron Waltzer: Hello good morning.

Tony Merola: Thank you, go right ahead.

Aaron Waltzer: So, good morning, my name is Aaron Waltzer I'm a Field Medical Director at Pfizer Dermatology within our Inflammation and Immunology Group. I am here today to ask to add Cibinqo abrocitinib to the PDL for the treatment of patients 18 years of age and older with moderate to severe atopic dermatitis. Cibinqo is a JAK inhibitor indicated for the treatment of adults with refractory moderate to severe atopic dermatitis which is not adequately controlled with other systemic drug products. This includes biologics or when use of their therapy is advisable. Limitations of use for Cibinqo included is not recommended in combination with other JAK inhibitors, biologic immunomodulators, or with other immunosuppressants. There is a black box warning inclusive for serious infections, mortality, major adverse cardiovascular events, and thrombosis. A contraindication includes antiplatelet therapies, exclusive of low dose aspirin during the first 3 months of treatment. Some common AE's include for subjects on the 100 and 200 mgs doses, nasopharyngitis, nausea, headache, herpes simplex, increased blood CPK, UTIs, vomiting or pharyngeal pain, influenza and gastroenteritis. The efficacy of Cibinqo is monotherapy in a combination with background topical corticosteroids was evaluated in 3 randomized placebo-controlled trials with 1,615 subjects, 12 years of age and older. In the monotherapy trial in patients with an IGA score of clear or almost clear and the reduction from the baseline was 44% and 38% with 200 once daily dose, 24% and 28% for the 100 daily dose, and 8% and 9% with placebo. The higher proportion of subjects in the Cibinqo monotherapy arms for both doses showed improvement in itching at week 12. In the combination therapy, trials in patients with an IGA of 0 almost cleared \_\_\_\_\_ 47% for 200 once daily, 36% for 100 once daily, and 14% for placebo. Cibinqo is recommended initial dose is 100 mg daily, 200 once daily as recommended for those who are not responding to the 100. It can be used with or without topical corticosteroids. In conclusion, atopic dermatitis continues to have a high unmet medical need and its costly to manage. To further manage this disease, we will need all agents available. Getting an orally administered medication will offer additional treatment options for patients with moderate and severe atopic dermatitis in New York State's Medicaid population. Thank you for your time.

Tony Merola: Thanks Aaron. Any questions? Hearing none, next speaker Yulia Rozovskiy.

Yulia Rozovskiy: Good morning, can you hear me?

Tony Merola: Yes, louder and clear, thank you.

Yulia Rozovskiy: Perfect. Thank you for the opportunity to speak here today. Good morning, my name is Yulia Rozovskiy, I'm a pharmacist in Organized Customer Field Medical Director with Pfizer covering rheumatology, gastroenterology and similar. Today, I will be focusing on the clinical updates on tofacitinib brand name Xeljanz from December 2021 which include

changes to the black box warning and a new indication of ankylosing spondylitis. Tofacitinib is indicated for the treatment of adult patients with active AS who have had an inadequate response and intolerant to one or more TNF blockers. Approved dose of tofacitinib is 5 mg twice daily or tofacitinib extended release 11 mg once daily. In the pivotal AS trial eligible patients had to have failed at least 2 NSAIDs and patients were randomized and treated with tofacitinib 5 mg twice daily or placebo for 16 weeks of blinded treatment followed by an open label phase for an additional 32 weeks. Primary endpoint with the proportion of patients who achieved an ACES 20 response at week 16. For results, patients treated with tofacitinib achieved greater improvements in ACES 20 and ACES 40 in response rates compared to placebo at week 16. Consistent results were also observed in a subgroup of patients who had an inadequate response to TNF blockers for both ACES 20 and ACES 40 endpoints at week 16. In terms of safety tofacitinib includes a black box warning for serious infections, mortality, malignancy, and thrombosis. In a large randomized close marketing safety study in rheumatoid arthritis patients 50 years of age and older was at least 1 cardiovascular risk factor, a higher rate of all-cause mortality and thrombosis was observed with tofacitinib compared to TNF blockers. In addition, in the same study, high rates of malignancies and major adverse cardiovascular events were observed with current or past smokers at additional increased risks. Most common side effects seen in clinical trials include upper respiratory infections, nasopharyngitis, diarrhea, and headaches. In conclusion, AS continues to have high and medical need and costs. To manage this deep need, alternative agents after TNF inhibitors and adding a medication with a novel mechanism of action and/or administration will offer an additional treatment option for patients with AS in New York Medicaid population. I respectfully ask the committee to add tofacitinib to the PDL for use. Thank you.

Tony Merola: Any questions for Yulia? Okay, hearing none, Dan Flores is in the next two speaker slots and is at the podium, thanks Dan.

Daniel Flores: Thank you. So, Dan Flores, PharmD, a former pharmacy director and now a member of Amgen's scientific global affairs team here to speak to the committee in support of Enbrel or etanercept systemic immunomodulator currently on the New York Medicaid PDL. Enbrel has been evaluated in clinical studies for 25+ years now, 20 years of real-world post marketing experience in moderate to severe rheumatoid arthritis. In addition to RA Enbrel is also indicated to treat juvenile idiopathic arthritis in patients 2 years of age and older. Moderate to severe plaque psoriasis down to the age of 4, psoriatic arthritis and ankylosing spondylitis. There is a box warning for this agent related to the risk of infection, as well as the risk of malignancies, that I'm fairly certain the board is aware of. Combined, the collective clinical experience of Enbrel adds up to over 3,000,000 patient years of exposure. Key update since our last review, in April of last year, the SEAM-PsA study was published. The study of etanercept and methotrexate in subjects with psoriatic arthritis was a 48-week multicenter double-blind study in patients with psoriatic arthritis who were naive to both biological demark as well as methotrexate, a total of 851 subjects were randomized to receive either Enbrel and methotrexate in combination. Enbrel as a single agent or methotrexate as a single agent. The primary



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endpoint of the study was the percentage of patients achieving an ACR 20 response at week 24 and a key secondary endpoint was minimal disease activity response at week 24. In SEAM-PsA, 65% of patients receiving Enbrel and methotrexate and 61% of patients receive Enbrel as monotherapy achieved the ACR 20 response at week 24 vs. just 51% of patients in the methotrexate monotherapy group. Proportion of patients achieving an MDA response at week 24 was also greater in the Enbrel combination and monotherapy groups compared to methotrexate monotherapy, 36% vs. 36% vs. 23% respectively. Safety in SEAM-RA was similar to that and has been recorded in the USPI. Also, referenced in my packet is the joint AADNPF guidelines for the treatment of psoriasis in pediatric patients listing Enbrel as an effective therapy for moderate to severe psoriasis in children 6 years of age and older. With that I want to thank you for your time and ask the Board to continue to cover Enbrel as a preferred agent. Any questions?

Tony Merola: Any questions for Enbrel? If not, we can transition Dan to your next topic thanks.

Daniel Flores: Perfect. I will transition to Apremilast, brand name Otezla, not currently on the New York Medicaid PDL but of interest covered by about three-quarters of the managed Medicaid plans here in New York State. Otezla is an oral small molecule agent unique in a number of categories. Decreases inflammation by inhibiting PDE4 intracellularly. Unique mechanism of action. Has no box warnings in this class. requires no baseline testing, no routine monitoring of labs during treatment. It is FDA approved for treatment of adult patients with active psoriatic arthritis. It is the first and only approved treatment for painful oral ulcers associated with Bechet's disease. It is now the only approved systemic agent approved for adult patients with plaque psoriasis regardless of severity; so, mild, moderate and severe plaque psoriasis. This recent label update is largely based on the advanced study referenced in my testimony template. Multicenter randomized placebo controlled double blind study where biologic naive adults with mild to moderate plaque psoriasis were randomized to receive Otezla or placebo for 16 weeks followed by a 16-week open label extension. Otezla dose 30 mg twice daily significantly and in a clinically meaningful way reduced psoriatic symptoms, improving scalp psoriasis, whole body itch compared to placebo with greater than 4 times the number of patients achieving a BSA 75 response vs. placebo at 16 weeks. Importantly, a tolerable safety profile maintained throughout the study. Also referenced is the study randomized placebo-controlled study of Otezla demonstrating significant improvements in patients with moderate to severe plaque psoriasis of the scalp at 16-weeks maintained out to 32-weeks. Lastly, I have referenced market scan real world cohort analysis conducted by Caplan and colleagues where 5,860 systemic naïve adult psoriasis patients who initiated either Otezla or methotrexate between the years of 2014 and 2019 were followed from 12 to 24 months. Patients initiating Otezla were found to be more adherent to their therapy. importantly, they also had a 58% lower likelihood of progressing to a biologic agent than those initiated on methotrexate potentially cost savings. Categorized as a systemic nonbiologic, Otezla is strongly supported by the guidelines. as I alluded to many managed Medicaid patients are already on this agent and that has ramifications

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to a unified PDL next year. So, for all of those reasons, I ask the Board to consider adding this agent to the PDL. Questions.

Tony Merola: Any questions for Dan, and I will also ask that Lane Anson start to approach the podium. Any questions for Dan on Otezla? Hearing none, we'll turn the podium over to Lane Anson.

Lane Anson: Good afternoon, everybody. My name is Lane Anson and I am a member of the Medical Value and Outcomes team with Sanofi Specialty Care. As a graduate of Albany College of Pharmacy, it's great to be back. I saw some familiar faces and some familiar scenery. I wanted to use my time to provide three brief updates on Dupixent or Dupilumab. The first in regard to the recent FDA approval an eosinophilic esophagitis or EOE in patients at least 12 years of age and weighing at least 40 kilograms. And secondly, I'd like to cover patient's recent approval in moderate to severe asthma patients 6 to 11 years of age. And then lastly, in atopic dermatitis patients 6 months to 5 years of age. So, Eosinophilic esophagitis occurs in about 1 in 1,000 patients and is a progressive inflammatory disease of the esophagus resulting in stenotic changes and narrowing of the esophagus. Traditional treatments that are not approved are dietary restrictions, swallowed corticosteroids, and dilation. The safety and efficacy of Dupilumab in eosinophilic esophagitis was demonstrated in TREAT study where it showed an improvement in both dysphagia symptoms as well as in eosinophil counts in the esophagus. Dupixent is the first approved biologic for this disease state. Secondly, just wanting to cover moderate to severe asthma patients 6 to 11 years of age. The Liberty Asthma Voyage trial demonstrated efficacy and no new safety signals in this population. And then lastly, regarding the very recent approval in atopic dermatitis patients 6 months to 5 years of age, the Liberty AD preschool study demonstrated efficacy in this population and no new safety signals were noted. Dupixent is the only approved systemic therapy in that 6 month to 5-year population. And with that, I'd like to open up if there are any questions and give the rest of my time back.

Tony Merola: Any questions for Lane? Hearing none, thank you. And the last two speaker slots are assigned to Elizabeth Lubelczyk.

Elizabeth Lubelczyk: Hi, good morning this is Elizabeth. Can you hear me?

Tony Merola: Yes, loud and clear.

Elizabeth Lubelczyk: Alright, great. So, good morning, my name is Elizabeth Lubelczyk and I am an Evidence and Outcome liaison with Eli Lilly Company. I will be providing testimony on Taltz. Ixekizumab is a humanized interleukin 17A antagonist indicated for the treatment of patients aged 6 years of age and older with moderate to severe plaque psoriasis who are candidates for systemic therapy or phototherapy. Adults with active psoriatic arthritis, adults with active ankylosing spondylitis, and adults with active non-radiographic axial spondylarthritis with objective signs of inflammation. Taltz is available at 80 mg of ixekizumab in 1 ml single dose prefilled auto injected or single dose prefilled syringe. Dosing varies based on indications. Please consult the prescribing information for all details related to dosing and administration. A

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citrate free formulation of ixekizumab has recently been investigated in two phase one, single blind studies in healthy participants that evaluated injection site pain, bio equivalence, and overall safety of the citrate 3 formulation of ixekizumab. Ixekizumab free formulation proved to be bio equivalent and associated with less injection site pain and had no other notable differences in the safety profiles compared to the original commercial formulation. A real-world evidence study was conducted to compare medication adherence persistent to monotherapy duration for ixekizumab vs. adalimumab, etanercept, eculizumab or ustekinumab with one to 3 year follow up in patients with psoriasis. Results from the study suggests that patient with psoriasis were significantly more persistent and more adherent to ixekizumab compared to other biologics in the real world. Ixekizumab treated patients remained on ixekizumab monotherapy significantly longer compared to those on other commonly prescribed biologics based on median time continuation. The most common adverse reactions associated with health treatment are injection site reactions, upper respiratory tract infections, nausea, and tinea infections. Please refer to the prescribing information for all other safety details. Thank you for the opportunity to address the Board this morning. and I'd be happy to take any questions.

Tony Merola: Any questions for Elizabeth on Taltz? Hearing none, Elizabeth you can transition to the next topic.

Elizabeth Lubelczyk: Okay. So, now I will be providing testimony on nasal Glucagon which is brand name Baqsimi. Baqsimi is an antihyperglycemic agent indicated for the treatment of severe hypoglycemia in patients with diabetes ages 4 years of age and older. Severe hypoglycemia is a medical emergency and is characterized by altered cognitive or physical functioning that requires assistance from another person for recovery. If untreated, severe hypoglycemia can lead to serious consequences such as loss of consciousness, seizure, coma and even death. Baqsimi is compact, affordable, and ready for use for nasal administration with no reconstitution required. The device contains a single dose of 3 mg of nasal glucagon powder and after administration, the nasal power is passively absorbed, and the dose does not need to be inhaled. Baqsimi does not require refrigerated storage, although it can be refrigerated or frozen for up to 24 months throughout its shelf life. It should be stored at temperatures up to 86-degree Fahrenheit and remain in the shrink wrap provided. Baqsimi has been studied in adults and children ages 4 years and above with type 1 diabetes and a small subset of adult patients with type 2 diabetes. Two studies conducted in adults demonstrated noninferiority to 1 mg of intramuscular glucagon in adult patients. The pediatric pharmacokinetic and pharmacodynamic study demonstrated similar glucose responses with nasal glucagon and intramuscular glucagon. A simulated rescue study was conducted to determine how trained caregivers or untrained acquaintances would administer nasal and injectable glucagon to mannequins in a simulation of unconscious people with diabetes in a severe hypoglycemic episode. Approximately 90% of both trained and untrained participants were able to administer Baqsimi successfully. In comparison, for the intramuscular glucagon group, 16% of the trained caregivers and none of the untrained acquaintances were able to successfully administer intramuscular glucagon. The most common adverse reactions are nausea, headache, vomiting, and upper respiratory tract irritation.

Please refer to the Baqsimi prescribing information for full details and safety information. And thank you again for the opportunity to address the Board, and I would be happy to take any questions.

Tony Merola: Any questions for Elizabeth? Hearing none that actually concludes the public comment period. I appreciate everybody's patience as we got a little bit of a late start due to technical issues and we are now using a phone that plugs into the wall, which is sort of unique at this day and age. So, with that said, Doug, I think we can move onto the pharmacy program update for today.

Doug Fish: Okay thank you, Tony. And just thanks to all the presenters that actually helped us get back on time by staying on time with all the speaker pieces. So, I think we've done a good job of making them up. Before we move to the next topic, I would just like to announce that there were no regulations review board recusals for today's meeting. So, no conflicts that were reported. Our first speaker is Kim Laurenzo from the Department on the Management of Physician Practitioner Administered Drugs. So, I'm going to turn it over to Kimberly.

Kimberly Laurenzo: Thanks Doug, good morning, everyone. My name is Kim Laurenzo and today I will be talking about the management of Practitioner Administered Drugs or PADS. We will start with a program overview and then we'll take a look at the current process in place for management of the drugs on the pharmacy benefit, followed by the program vision and benefits, and a look at the roadmap to implementation. We will end with the summary and resources and time for any questions.

Doug Fish: Kim, you may just want to move the microphone a little bit closer.

Kimberly Laurenzo: Is that better?

Doug Fish: Yes.

Kimberly Laurenzo: Okay, so starting with the program overview. Establishing parity and uniform clinical standards for coverage of drugs was an administrative action item in the 22/23 enacted Medicaid budget. Currently drug coverage in the fee for service program falls into two separate buckets; drugs that are typically self-administered and dispensed by a pharmacy are reimbursed through the pharmacy benefit, and drugs that are typically administered by a healthcare practitioner and billed by the provider are covered under the medical benefit. There is an area of overlap that includes drugs and drug classes that could fit the description of both pharmacy and medical. A good example of this would be the systemic immunomodulators class. This class contains several drugs that have both self-administered and practitioner administered formulations. Because of the disparity between management of drugs on the pharmacy benefit vs. the medical benefit, this can lead to the same drugs facing very different clinical criteria and claims processing depending on how and where it is administered.

Now we will take a look at some of the different between pharmacy and medical drug claims. Pharmacy drug claims are billed prospectively giving an opportunity for the provider to change

therapy before the drug is given. Pharmacy claims are also submitted electronically and go through automated clinical criteria which results in a real time claim response and quick reimbursement. In contrast, medical claims are billed retrospectively. This means billing is done after the medication has already been administered to the patient and the opportunity to change the drug therapy has been missed. Medical drug claims needing clinical review are submitted manually on paper and reviewed manually which results in an off-line claim response and could result in delays in reimbursement. The program goals are to ensure patient safety and clinically appropriate use of medications to create a standard process for developing and implementing coverage criteria across the pharmacy and medical benefits to modernize the way drug claims are submitted on the medical benefit, and to improve efficiency of the claims review process for drugs covered under the medical benefit. These goals can be achieved by leveraging well proven processes that are already in place on the pharmacy benefit.

Next, we'll take a more detailed look at the current process for management of drugs on the pharmacy benefits. The process begins with clinical criteria development. Drugs are covered by Medicaid for FDA approved uses in accordance with FDA package labeling or compendia supported uses. If a drug or drug class is identified as needing additional clinical criteria to ensure safe, appropriate, and cost-effective use, that drug is brought for review by the DUR Board which is a process all of you are very familiar with. Once the DUR Board votes on recommendations, the Commissioner of Health provides the final determination, and clinical criteria are published on the PDL and implemented using RxPert. RxPert is a system administered by our clinical editing vendor Kepro and it is an automated prior authorization adjudication system that looks back into a patient's claim history to determine if clinical criteria for a prescribed drug are met. It was implemented for pharmacy drug claims in December of 2011. The flow starts with the pharmacy submitting a claim, the information on the claim goes through the RxPert system to search that patients previous claim history to look for information that may satisfy clinical criteria requirements on that drug. This could be diagnosis codes, prior drug therapy, office visits, laboratory tests, among many other things. If clinical criteria requirements are found, the claim pays automatically at point of sale and the pharmacy dispenses the drug. If clinical criteria are not met, the prescriber has the option to adjust or change the prescribed therapy or contact the Magellan call center to request prior authorization.

Moving onto the program vision and benefits. The program vision is to take the current process for review of drugs and implementation of clinical criteria on the pharmacy benefit and leverage that into a new and improved process for drugs on the medical benefit. This will enable the fee for service program to have one standard approach to the management of all drugs.

Program benefits for providers include increased transparency into covered criteria, ability to secure authorization prior to drug administration, decreased administrative burden, which will come from a streamline clean submission process and expedited reimbursement. Patients will benefit from improved safety checks that will ensure medication use is appropriate and in line with current recommendations.

Moving onto the Roadmap. We are at the beginning stages of this initiative, but to give a general idea of the activities that will occur leading up to implementation, here is a look at the roadmap. We have started the process of developing clinical criteria for PADS to bring them in-line with clinical criteria that are already implemented on the pharmacy benefit. As you probably noticed, there are 4 DUR topics being covered later today involving PADS. While we are working through the process of developing criteria, we will also be working on system enhancements that will enable the use of audible clinical editing for medical claims. As we get closer to our go-live date, which is still to be determined, the department will undergo a robust communication plan to prepare providers for this change in process. It is important to note that clinical criteria for PADS will be published in drug coverage policies once recommendations are approved, but they may not be fully implemented until the future go-live date when systems are in place.

Moving onto the summary and resources. In summary, uniform clinical standards for coverage of drugs will modernize the process for review of drugs under the medical benefit. Existing tools and processes in place on the pharmacy benefit will be leveraged. Clinical criteria will be established for PADS and will be brought to the DUR Board for review when needed. And more information on timeline and details regarding implementation will be provided as they become available.

This slide has helpful resources on it. And now I'll take any questions.

Doug Fish: Any questions for Kim? Thank you.

Tony Merola: Okay, I don't hear any. I will mention that these slide sets or slide decks that you're seeing today, they are actually already up on our website. I know that question always come about, can we see these slide sets? They are inside the WebEx, the WebEx is archived as Doug said, but they are also actually currently posted on our website so you can get to them if you're looking for them as reference. So, before we leave that update, I will just see if there's any questions before we move onto the Preferred Drug Program reviews. Okay, hearing none, we'll move onto the next section of the agenda which is the Clinical Reviews under the Preferred Drug Program the fee for service drug program. So, let's just do an audio check with Mina Kwon from Magellan.

Mina Kwon: Hi, good morning, everybody can you hear me, okay?

Tony Merola: Yep, loud and clear Mina. So, let me just introduce the topic and then you can take it from there.

Mina Kwon: Okay, great.

Tony Merola: So, as mentioned earlier today, there are three classes with new clinical information since the previous review. Those are antipsychotics injectable, antipsychotics second generation, systemic immunomodulators, and then a new class, Glucagon agents. Mina will be taking us through the new clinical information associated with those classes. So, Mina, I think you can take it over from there.

Mina Kwon: Okay, perfect, thanks, Tony. Good morning, everybody. The first class we will be reviewing today is antipsychotic injectables. So, for new clinical information in the class, we have a new drug Invega Hafyera or Paliperidone Palmitate. So Invega Hafyera is an atypical antipsychotic indicated for the treatment of schizophrenia in adults after they have been adequately treated with either a once-a-month paliperidone extended-release injectable suspension for at least 4 months or an every 3-month paliperidone extended-release injectable suspension which is the Invega Trinza for at least one three-month cycle. It's available as an extended-release injectable suspension in two different strengths, single dose prefilled syringes and it is to be administered by gluteal injections once every 6 months by a healthcare professional and not to be administered by any other route.

Contraindications and warnings include any known hypersensitivity to paliperidone, risperidone or to any excipients. Cardiovascular adverse reactions in elderly patients with dementia related psychosis, neuroleptic malignancy syndrome, QT prolongation, tardive dyskinesia, metabolic changes, orthostatic hypotension and syncope, leukopenia and neutropenia and agranulocytosis, hyperprolactinemia, potential for cognitive and motor impairment, and seizures.

Common adverse drug reactions to this product are upper respiratory tract infections, injection reaction, weight increase, headaches, and Parkinsonism.

Invega Hafyera is to be avoided with use with strong CYP3/AA and/or P glycoprotein inducers during the dosing interval. Administered with a strong inducer is necessary to consider managing the patient using the paliperidone extended-release tablets. For specific populations and pregnancy, it may cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure. And the drug is not recommended with patients with renal impairment. There was a clinical comparative study within class and the study demonstrated noninferiority of Invega Hafyera in to Invega Trinza in the treatment of schizophrenia.

So, here's the PDL snapshot of what the antipsychotic injectable class looks like today. To recap, we discussed a new drug Invega Hafyera which is an every 6-month injectable atypical antipsychotic indicated for the treatment of schizophrenia in adults after they have been adequately treated with either Invega Hafyera for at least 4 months or Invega Trinza for at least one cycle. There was a clinical comparative study comparing efficacy with Invega Trinza which demonstrated Invega Hafyera to be noninferior. Currently, Invega Sustenna and Trinza are preferred on the PDL and Invega Hafyera is non-preferred on the PDL. This concludes this class review. Are there any questions or comments?

Tony Merola: Any clinical questions for Mina? Again, all classes will be reviewed from a financial perspective in executive session, but at this time, are there any clinical questions on this drug class?

Asa Radix: I just have one question if possible. Is there any data to show if the prolactin levels are less with the Hafyera compared to the other Invega Trinza?

Mina Kwon: You said the prolactin levels.

Asa Radix: Prolactin levels are any different in terms of their elevation.

Mina Kwon: I didn't see that in the study, but I could go and relook at it for you and get back to you on that.

Tony Merola: And that question came from Asa. Is that correct?

Asa Radix: Yeah, sorry about that, it's Asa.

Tony Merola: Okay, thank you. Any other questions for Mina? Okay, I think we can move onto the antipsychotic second generation.

Mina Kwon: Okay, so the next class we will be reviewing today are antipsychotics second generations. For new clinical information on this class, we have a new drug Lybalvi which is olanzapine and samidorphan. We are also going to go over new indications for Caplyta, lumateperone, and Rexulti brexpiprazole.

Lybalvi is a combination of olanzapine an atypical antipsychotic and samidorphan an opioid antagonist indicated for the treatment of schizophrenia in adults and also for Bipolar 1 disorder in adults. For Bipolar 1, it could be used as acute treatment in manic or mixed episodes as monotherapy and also as an adjunct to Lithium or Valproate. It can also be used as maintenance monotherapy treatment. Olanzapine, as discussed before, it's available I'm sorry Lybalvi is available in four different strengths and samidorphan component is all the same at 10 mg. It's the ONP component that differs at 5, 10, 15 and 20 mg. And that's to be taken once daily with or without food.

Lybalvi is contraindicated in patients using opioids and patients undergoing acute opioid withdraw due to an opioid antagonist component. And warnings and precautions include cerebrovascular adverse reactions in elderly patients with dementia related psychosis. Resuscitation of opioid withdrawal in patients who are dependent on opioids or liability to life threatening opioid overdose, neuroleptic malignant syndrome, drug reaction with eosinophilia and systemic symptoms, metabolic changes, tardive dyskinesia, orthostatic hypotension and syncope, leukopenia, neutropenia, agranulocytosis, seizures, potential for cognitive and motor impairments, anticholinergic effects, and hyperprolactinemia.

There is a black box warning for Lybalvi; elderly patients with dementia related psychosis treated with antipsychotic drugs are at increased risk of death. Lybalvi is not approved for treatments of patients with dementia related psychosis. The most common adverse drug reaction seen with Lybalvi was weight increase, somnolence, dry mouth, and headache. Some common adverse drug reactions we see with olanzapine when treated in bipolar disorder is asthenia, dry mouth, constipation, increased appetite, somnolence, dizziness, and tremors. And if olanzapine is used in adjunct to Lithium or valproate other common ADRs are dry mouth, dyspepsia, weight



gain, increased appetite, dizziness, back pain, constipation, speech disorder, increased salivation, amnesia, and paresthesia.

So Lybalvi is not recommended for use with strong CYP3AA inducers if used with a strong CYP1A2 inhibitors, dosage reduction of olanzapine component should be considered. If used with a CYP1A2 inductor, doses increased of olanzapine component should be considered. If Lybalvi is used with CNS acting drugs, this may potential orthostatic hypotension. When used with anticholinergic drugs, this can increase the risk for severe GI reactions. Blood pressure should be monitored if used with antihypertensive agents and Lybalvi is not recommended for use with levodopa or dopamine agonists.

For specific populations, pregnancy may cause extrapyramidal and withdrawal symptoms in neonates with a trimester exposure and use is not recommended in patients with end stage renal disease. There was a clinical comparative study that evaluated weight changes in patients with schizophrenia and treatment with Lybalvi was associated with statistically significant less weight gain than treatment with olanzapine alone and with a smaller proportion of patients who gained greater than or equal to 10% of body.

Now we will go into new indications. So, Caplyta is now indicated for depressive episodes associated with Bipolar 1 or 2 disorder for Bipolar depression in adults as monotherapy and also as adjunctive therapy with Lithium or valproate. It is also available in 2 new strengths: 10.5 and 21 mg capsules. Prior, it was only available in the 42 mg capsules. And the new dosage form allows for dosage modifications and hepatic impairment and also for drug interactions.

Rexulti, the FDA has expanded the indications to include treatment of schizophrenia in pediatric patients 13 to 17 years old. previously it was only indicated for use in adults. Starting recommended and max dose is listed here. The label now also includes a long-term open label study in pediatric patients with schizophrenia, 2.7% of pediatric patients with normal baseline fasting glucose experienced a shift from normal to high when taking Rexulti.

So here is a PDL snapshot of what the antipsychotic second generation site looks like today. To recap, we discussed a new drug Lybalvi which an oral combination of olanzapine an atypical antipsychotic and samidorphan an opioid antagonist indicated in the treatment of schizophrenia and Bipolar 1 disorder in adults. Currently Lybalvi use is non preferred on the PDL. Due to its opioid antagonist component, Lybalvi is contraindicated in patients using opioids and patients undergoing opioid withdrawal. Lybalvi promotes antipsychotic efficacy seen with olanzapine with less weight gain. On the PDL as a preferred agent, we have oral Olanzapine that shares the FDA approved indications of Lybalvi for the treatment of schizophrenia and Bipolar 1 disorder along with other second generation atypical antipsychotic options that are shown here that are approved for the treatment of both indications as well. We also went over the indications for Caplyta and Rexulti which are both non preferred agents. Caplyta is now FDA approved for Bipolar depression in adults as monotherapy and as adjunctive therapy with Lithium or valproate and has new strengths approved for adult's adjustment to severe hepatic impairment and drug

interactions. Previously it was approved for schizophrenia only. Currently we have Latuda and Quetiapine that can be used for Bipolar depression. Rexulti now has an expanded indication for the treatment of schizophrenia in patients aged 13 and up, and the label was updated with the warnings on metabolic fasting glucose changes within the pediatric population. Currently we have Quetiapine, aripiprazole, olanzapine, and risperidone preferred on the PDL for schizophrenia treatment in patients 13 and up.

This next slide has more criteria for certain drugs within the class which you can find on the posted PDL that wouldn't fit all on one page. That concludes this section. Are there any questions or comments?

Tony Merola: Just for clarification, those last two slides are just snapshots of our current PDL. So, it's out there on the public website also. So, any questions for Mina on the antipsychotic second generation?

Jadwiga Najib: No questions. This is Jadwiga but I just have a comment. Thank you for the presentation. The comment on the ability of samidorphan with olanzapine and low weight gain is a great finding but, I just think the apparent lack of its effect on various metabolic variables really pose the question, is clinical significance indication of weight gain in patients? Because olanzapine affects a lot of neuropeptides associated with appetite control and energy metabolism like leptins, relin and so, I just think that the ideal of that the additional agent is not really treating the psychiatric condition but rather treating the side effect of the psychiatric drug with another drug. And I think that some physicians already use metformin and even aripiprazole to decrease the effect of the weight gain. Just my comments.

Tony Merola: Thank you.

Mina Kwon: According to my notes, it's not a weight loss drug marketed as mentioned before you just see less weight gain but it's not a weight loss drug.

Tony Merola: Any other questions for Mina. Okay so now we'll move to the immunomodulators for the systemic immunomodulator as we call them. So, Mina has some updates for us, and Linda Catanzaro also has some guideline updates. Mina will take us through the new drugs or indication updates, and then after Mina's presentation, Linda Catanzaro from SUNY Buffalo will take us through the updates we have on atypical dermatitis clinical criteria because there have been new guidelines since the previous review of the class. So, Mina, you can take it away and then we'll hand it over to Linda after you complete your presentation.

Mina Kwon: Okay, thank you, Tony. So, the third and rather large class we have today that we'll be reviewing is immunomodulators systemic.

So, for new clinical information in this class, we have two new drugs Cibinqo abrocitinib and Adbry tralokinumab. We are going to be going over new indications for these products, new practice guidelines and key label revisions, and we'll also be going over a few studies.

Cibinqo is a Janus kinase or JAK inhibitor indicated for the treatment of adults with refractory moderate to severe atopic dermatitis whose disease is not adequately controlled with other systemic drug products including biologic or when use of those therapies is inadvisable. Cibinqo is not recommended for use in combination with other JAK inhibitors, biologic immunomodulators, or with immunosuppressants. It is available as an oral tablet in 3 different dosage forms 50, 100 and 200 mg. The recommended dose is 100 mg once daily and 200 mg once daily if recommended for patients who are not responding to 100 mg. There are some dosing recommendations for patients with moderate renal impairment and those who are poor CYP2C19 metabolizers.

Cibinqo is contraindicated with antiplatelet therapies except for low dose aspirin at a dose less than or equal to 81 mg daily during the first 3 months of treatment. Lab abnormalities may occur, so lab monitoring is recommended to check potential changes in platelets, lymphocytes and lipids. All vaccines should be avoided prior to and immediately after treatment. Cibinqo shares a black box warning with all JAK inhibitors with serious infections, mortality, malignancy, major adverse cardiovascular events, and thrombosis.

So, the most common adverse drug reaction being in subjects receiving 100 mg and 200 mg dosage were nasopharyngitis, nausea, headache, herpes simplex, increased blood creatin phosphokinase, dizziness, urinary tract infections, fatigue, acne, vomiting, oropharyngeal pain, influenza, and gastroenteritis. Some common adverse drug reactions seen in subjects on either 100 mg or 200 mg include impetigo, hypertension, contact dermatitis, upper ab pain, ab discomfort, herpes zoster, and thrombocytopenia.

There are drug interactions with strong inhibitors CYP2C19 so a dosage of 50 or 100 mg once daily is recommended. Cibinqo is to be avoided in use with moderate to strong inhibitors of both CYP2C19 and CYP2C9 or with strong CYP2C19 or CYP2C9 inducers. For P-glycoprotein substrate where small concentration changes may lead to serious or life-threatening toxicities, patient monitor and titrate the dose of the P-gp substrate.

For specific populations, breastfeeding is not recommended with the use of Cibinqo and Cibinqo is to be avoided in patients with severe renal impairment or end stage renal disease, and also with patients with severe hepatic impairment.

Adbry is the next new drug we will be discussing. And Adbry is an interleukin-13 antagonist indicated for the treatment of moderate to severe atopic dermatitis in adult patients whose disease is not adequately controlled with topical prescription therapies or when those therapies are not advisable. Adbry can be used with or without topical corticosteroids. It is available as a subcutaneous injection 150 mg/ml solution in a single dose prefilled syringe with needle guard. The initial loading dose is 600 mg which is four the 150 mg injections followed by 300 mg which is two of the 150 mg injections administered every other week. In a dose of 300 mg every four weeks can be considered for patients weighing below 100 kilograms will achieve clear or almost clear skin after 16 weeks.

For contraindications, any known hypersensitivity to the product or any excipients. There are warnings for conjunctivitis and keratitis, parasitic infections, and risk of infection with live vaccine. The most common adverse drug reactions seen were upper respiratory tract infections, conjunctivitis, injection site reactions, and eosinophilia.

Drug interactions have not been assessed with Adbry and in specific populations in pregnancy there is limited data however human IgG antibodies are known to cause the placental barriers, therefore Adbry may be transmitted from the mother to the developing fetus. There is no lactation data and safety, and efficacy has not been established with pediatrics.

So, now we are going to be going over new indications for the products since our last review. The first one we have is Duplixent dupilumab is now indicated for the treatment of adult and pediatric patients aged 6 months and older with moderate to severe atopic dermatitis, previously indicated for atopic dermatitis in patients 6 and up. Duplixent is also now indicated for the treatment of adult and pediatric patients aged 12 and up weighing at least 40 kilograms with eosinophilic esophagitis. Duplixent also has an expanded indication of add-on maintenance treatment for moderate severe asthma in patients aged 6 and older, previously was indicated for those 12 and older.

Olumiant or baricitinib now has a new indication for treatment of COVID-19 adults hospitalized requiring supplemental oxygen, noninvasive or invasive mechanical ventilation, or extracorporeal membrane oxygenation. Olumiant is also not indicated for the treatment of adult patients with severe alopecia areata.

The next product is Nucala mepolizumab now is indicated as an add-on maintenance treatment of adult patients 18 and older with chronic rhinosinusitis with nasal polyps.

Skyrizi risankizumab is now indicated for the treatment of active psoriatic arthritis in adults and also for treatment of moderately to severely active Crohn's disease.

Otezla apremilast is now indicated to treat mild to moderate plaque psoriasis. Previously it was indicated for moderate to severe.

Cosentyx secukinumab has an expanded indication to include active juvenile psoriatic arthritis in patients 2 and up. Previously it was only indicated for adults. Cosentyx also has a new indication for active enthesitis-related arthritis in patients 4 and up. Cosentyx also has an expanded use for moderate to severe plaque psoriasis in patients who are candidates for systemic therapy or phototherapy to include patients greater than or equal to 6 years of age, previously was only approved for use in adults.

Orencia abatacept indication for prophylaxis of acute graft versus host disease in combo with calcineurin inhibitor and methotrexate in adults and pediatrics who would up undergoing stem cell transplantations.

Xeljanz tofacitinib is now indicated for treatment of adults with active ankylosing spondylitis that had inadequate response or intolerance to one or more TNF blockers.

Rinvoq upadacitinib now can be used in adults with active ankylosing spondylitis who have had inadequate response or intolerance to one or more TNF blockers. It also can be used for treatment of adult patients with moderately severe active ulcerative colitis who have had inadequate response to intolerance to one or more TNF blockers. It also has an indication for treatment of adult and pediatric patients 12 and up with refractory moderate to severe atopic dermatitis. And the final new indication for Rinvoq is for treatment of adults with active psoriatic arthritis who have had inadequate response or intolerance to one or more TNF blockers.

We will now move onto some practice guideline updates. The American College of Rheumatology states that systemic juvenile idiopathic arthritis without macrophage activation syndrome, biologic disease modifying antirheumatic drugs or DMARDs are conditionally recommended as initial therapy and although there is no preferred agent, these are strongly recommended over the convention DMARDs.

The American Gastroenterological Association published guidelines for the management of moderate to severe luminal and fistulizing Crohn's disease in adult outpatients. They recommend the anti-TNF therapy over no treatment for induction and maintenance for remission.

So, now we are going to go over some comparative studies within class. There was a trial comparing Cosentyx with Humira. EXCEED study assessed the efficacy of Cosentyx and Humira for the treatment of adults with active psoriatic arthritis and the primary endpoint analyzed superiority of Cosentyx over Humira was not met.

The second study, there was a study comparing Stelara and Humira. The previous study evaluated the efficacy and safety of Stelara and Humira in adult patients with moderately severe active Crohn's disease who were biologic naïve. And there was no statically significant difference found in clinical remission rates at week 52, which was the primary endpoint between patients treated with Stelara and those treated with Humira.

So now we have key label revisions. Duplixent has addition of angioedema and facial skin reactions, information on the conjunctivitis and keratitis adverse drug reactions from post marketing data.

Orencia's label now includes clinical considerations for live vaccines and infants exposed to it. And an addition of a warning section for cytomegalovirus and Epstein Barr virus reactivation in acute graft versus host disease.

So, the next 3 are JAK inhibitors. Olumiant, Rinvoq and Xeljanz and they all now include a box warning update to include information about increased risks of serious heart related events, cancer, blood clots, and death.

Rinvoq also modified its rheumatoid arthritis component on the label to include inadequate response or intolerance to 1 or more TNF blockers.

Xeljanz rheumatoid arthritis, psoriatic arthritis, and polyarticular juvenile idiopathic arthritis is revised to include an inadequate response or intolerance to one or more TNF blockers.

Here is our PDL snapshot of what the immunomodulators systemic class looks like today. To recap, we assessed two new drugs Cibinqo and Adbry both indicated for moderate to severe atopic dermatitis whose disease is not adequately controlled. Cibinqo is an oral JAK inhibitor taken daily and Adbry is a subcutaneous injection interleukin antagonist administered every other week after the loading dose. They have the same class black box warnings of all JAK inhibitors with serious infections, mortality, malignancy, major adverse cardiovascular events, and thrombosis. There are no clinical comparative studies in this class for either Cibinqo or Adbry and they are both non-preferred on the PDL.

Currently on the PDL, we have Dupixent preferred which is an interleukin 4 and 13 inhibitor subQ agent indicated for moderate to severe atopic dermatitis with disease not adequately controlled with topical therapies in patients 6 months and older which is different from Adbry and Cibinqo which is only approved in adults.

For the new indications, we had a few for Dupixent which are superior agents on the PDL. We also discussed new indications for Ilumya for use in treatment of hospitalized adults with COVID-19 requiring oxygen which Actemra has a similar FDA approval for in its IV form which is not reviewed. Ilumya also has a new indication for severe alopecia areata which is an autoimmune disorder causing patchy baldness. Ilumya is the first systemic treatment for alopecia areata.

Skyrizi's new indications for psoriatic arthritis covered by preferred agents Cosentyx, Enbrel and Humira, and Crohn's new indication overlaps with Humira as well.

Otezla's new indications are mild to moderate plaque psoriasis as different from the other immunomodulators which treat moderate to severe plaque psoriasis.

Orencia's new indication for youth and acute graft versus host disease overlaps with Enbrel's compendia use which is preferred.

Xeljanz now has a new indication for ankylosing spondylitis in patients who have had inadequate response to one or more TNF blockers who do not have any JAK inhibitors such as Xeljanz was preferred. The Cosentyx as an interleukin inhibitor that can be in AR but is not a TNF blocker and is preferred.

Rinvoq also had a new indication for ankylosing spondylitis for those with inadequate response to one or more TNF blockers and new indications for ulcerative colitis, atopic dermatitis, and psoriatic arthritis covered by agents that we have in preferred status that we just discussed for those indications.

That concludes this class review. I'll take any questions or comments.

Tony Merola: Any questions for Mina on her information before we transition to Linda Catanzaro? Okay so referring to the slides, slide 15, Linda Catanzaro's focus is down at that atopic dermatitis line and the indication specific requirements there. So, I'll just ask Georgia to pull up Linda slide deck on atopic dermatitis. And then Linda, while we do that, just looking for an audio check from you.

Linda Catanzaro: Good afternoon, can everyone hear me, okay?

Tony Merola: It could be a little bit better, but I would say we hear you okay.

Linda Catanzaro: Alright I'll try to speak up. Is that better?

Tony Merola: Yes.

Linda Catanzaro: Okay. So, I am going to review, as mentioned the systemic immunomodulators specifically indicators for atopic dermatitis and we're just going to take a look at the preferred drug with clinical criteria data.

So, this is just a summary slide showing the four agents that were already mentioned within the systemic immunomodulators category. These are the four agents with FDA approval for treatment of atopic dermatitis. Dupixent, or dupilumab, is an interleukin 4 receptor alpha antagonist that was approved in 2017 for atopic dermatitis. The FDA indication is for moderate to severe disease not adequately controlled with topical prescription therapies. It is now approved for patients aged 6 months and up. It is available in single-dose syringes and pens and the usual adult dose is a 600 mg loading dose followed by 300 mg every other week. Weight-based dosing is indicated for ages 6 months to 17 years.

Tralokinumab, or Adbry, is an interleukin 13 antagonist and has the same indication as Dupixent. So, both of these are biologic agents indicated for moderate to severe atopic dermatitis. It is approved for use in adults and also available in single dose syringes and pens for subcutaneous injection and also has the usual dose of a 600 mg initial dose followed by 300 mg every other week.

The next two drugs listed here are abrocitinib and upadacitinib that are both Janus kinase inhibitors and both have the same indication for refractory moderate to severe atopic dermatitis not adequately controlled with systemic drug products, including biologics, or when such therapies are not advised. Abrocitinib is approved for adults and available as oral tablets dosed at 100 mg once daily which may be increased to 200 mg if response is inadequate. And upadacitinib is approved for ages 12 years and up and available as extended-release oral tablets. 15 mg once daily is the usual dose and may be increased to 30 mg if response is inadequate. Also, as stated previously, the JAK inhibitors carry a boxed warning for serious infections, mortality, malignancy, major adverse cardiovascular events, and thrombosis. Any questions?

So this is just an excerpt of what we just saw with the whole class of systemic immunomodulators on the PDL but it just shows that of these four agents, Dupixent is preferred and Adbry, Cibinqo, and Rinvoq are non-preferred; and prior authorization criteria include a confirmation of diagnosis for an FDA or compendia-supported use, and step therapy indication-specific requirements for atopic dermatitis require a trial with a medium or high potency topical steroid and one other topical prescription agent other than a steroid for a combined duration of at least 6 months prior. So, this applies to all four agents and clinical criteria and step therapy were implemented for dupilumab in 2017 and tralokinumab was added after FDA approval in 2021 and abrocitinib and upadacitinib were added after FDA approval in 2022.

So, with regard to topical prescription agents other than steroids, those that are FDA approved for atopic dermatitis include crisaborole, or Eucrisa, which is a phosphodiesterase-4 inhibitor indicated for mild to moderate atopic dermatitis in ages 3 months and up. Pimecrolimus, or Elidel, is a calcineurin inhibitor indicated as a 2<sup>nd</sup> line therapy for short-term non-continuous treatment of mild to moderate atopic dermatitis 2 years and up. Ruxolitinib, or Opzelura, is a Janus Kinase inhibitor indicated for short-term non-continuous treatment of mild to moderate atopic dermatitis not adequately controlled with topical prescription therapies for patients 12 years and up. And tacrolimus, or Protopic, is another calcineurin inhibitor indicated as 2<sup>nd</sup> line therapy for short-term non-continuous treatment of moderate to severe atopic dermatitis in ages 2 years and up.

So, in the next few slides we are going to quickly review the clinical guidance that has evolved since the initial implementation of the current clinical criteria. So, the American Academy of Dermatology is publishing a new series of atopic dermatitis guidelines which will supersede the 2014 guidelines. The first update was published in January of this year and focuses on awareness of comorbidities associated with atopic dermatitis in adults and contains no updated guidance on treatments, other than mentioning that some agents have multiple indications that can be potentially beneficial for patients with those comorbidities.

The 2014 guidelines recommended systemic immunomodulatory agents for patients with signs and symptoms not adequately controlled with optimized topical regimens and/or phototherapy. Data was insufficient to form recommendations on any agent and those guidelines were published prior to FDA approval of the targeted therapies for atopic dermatitis.

So, at the end of 2017, can everyone still hear me, okay?

Tony Merola: Yeah, Linda, anything you can do to maybe move the mic closer to you would be great, but we can still hear you.

Linda Catanzaro: Is this better.

Tony Merola: Yes, very much so.

Linda Catanzaro: Okay sorry about that. Okay so at the end of 2017, an expert perspective on management of moderate to severe atopic dermatitis was published and this was a



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multidisciplinary consensus of US practitioners addressing current and emerging therapies for atopic dermatitis specifically matters to severe. The guidance relevant to our clinical criteria reviewed today include the following points, that you defined treatment failure as one of any of the following despite the appropriate dose, duration, and adherence to a therapeutic agent. Inadequate clinical improvements, failure to achieve stable long-term disease control, presence of ongoing impairment or unacceptable adverse effects or intolerability. They also noted that there was no generalizable time to demonstrate efficacy of topical treatments however, they recommended a regimen duration of up to 4 weeks for active treatment, and 2 to 3 times weekly to prevent recurrence noting that some patients and body sites may require more than 4 weeks treatment.

On the role of emerging biologics, they recommended dupilumab as a first line systemic treatment in adults with moderate to severe atopic dermatitis who are uncontrolled with topical therapies. At that time, it was only approved in adults. And noted that the safety and efficacy of future biologics of small molecules needed to be evaluated to determine the place of therapy. rationale for recommending dupilumab as a 1<sup>st</sup> line was due to the safety profiles of conventional systemic therapies and these included several agents that are not approved for atopic dermatitis.

Subsequently, in 2018, the American College of Allergy, Asthma, and Immunology published an atopic dermatitis yardstick which is practical recommendations for an evolving therapeutic landscape. And this table just summarizes key points from the step care management recommended in that yardstick based on severity, and acute or maintenance treatments. So, they recommend using shared decision making for treatment decisions, and you will see for the moderate and severe categories, in the moderate severity basic management atopic anti-inflammatory medications are recommended including maintenance topical corticosteroids, or maintenance topical calcineurin inhibitors or Crisaborole. And for severe basic management and referral to a specialist is recommended with the options of phototherapy to be considered, dupilumab and systemic immune suppressant as well as considering acute treatments for some patients. They also give guidance on the use of topical corticosteroids for acute treatment and recommend considering topical calcineurin as well as Crisaborole. So, they noted that before stepping up, patients should be reassessed for appearance, potential comorbidities, and also confirming that increased symptom level is due to atopic dermatitis and when stepping up from either mild to moderate treatment or moderate to severe treatment, they recommend a 3-month therapeutic trial with reassessment at 4 to 8 weeks. There is also a flow diagram within this document that states that stepping up from moderate to severe levels of treatment for patients that are. Are you getting some feedback there?

Tony Merola: Just a little bit.

Linda Catanzaro: We are hearing it here but nothing's different. Okay, I'll keep going. So, it's recommended that the aggressive force of topical prescription therapy with topical corticosteroid and/or topical calcineurin inhibitor or Crisaborole for at least 3 weeks following basic management and avoidance of triggers, etc. and referral to a specialist being recommended.

So, the last piece of clinical guidance to include in review today is current living systemic review and network meta-analysis of systemic immunomodulatory treatments for atopic dermatitis. This is published by in JAMA Dermatology originally in April of 2020 and then updated this past March in 2022. So, by living it connoting that the updated searches performed every 4-months and the updates are made available online. So again, for the objective of this network meta-analysis was to compare reported measures of efficacy and assessment of clinical safety and clinical trials. They searched Conference Central Register, Medline, Mbase and other data bases through June 15<sup>th</sup> of 2021 for this most recent update. Selected randomized clinical trials of at least 8-week treatment duration for moderate to severe atopic dermatitis. Main outcomes included changes in eczema area and severity index, patient already on eczema measures, Dermatology Life Quality Index and Peak Pruritis Numeric Rating Scale. So, there were a total of 60 trials with over 16,000 patients most in adults receiving up to 16 weeks of therapy and most were compared to placebo. Authors noted there was insufficient data to conduct the analysis in children. So, this table just summarizes the results for the 5 targeted therapies for 8 to 16 weeks of treatment in adults with moderate to severe AD and this was started primarily from an additional 21 studies that were included and added to the March update. So, this table just summarizes the results of the comparison of reductions in the EASI scores and the various treatments listed are compared to the regimen of dupilumab 600 mg initially followed by 300 mg every other week. So, they show the mean differences in the reductions of EASI scores. And I will just highlight that abrocitinib 200 mg and upadacitinib 30 mg you can see the positive mean difference that shows that they had a greater reduction in the EASI scores compared to dupilumab however, these were small. They are just statistically significant. All the results were small changes in the EASI scores. So Upadacitinib 15 mg once daily was similar to dupilumab and the Baricitinib strength as well as Tralokinumab were slightly worse in being able to reduce EASI scores. Overall, the pattern of results compared for EASI was similar with the other indexes and the authors concluded that abrocitinib and Baricitinib, Upadacitinib and Tralokinumab were associated with comparable improvements, noting that the differences were small in index scores compared to dupilumab for moderate to severe atopic dermatitis. Data is still accumulating so this is an ongoing process of updating the data and the evidence as it becomes available and could aid in shared decision making for treatments.

So, we did do a review of comparator state Medicaid programs to look at the preferred drug list criteria. And the 9 states we looked at were California, Colorado, Florida, Illinois, Massachusetts, Michigan, Pennsylvania, Texas, and Washington. Dupixent is a preferred drug for atopic dermatitis in 4/9 states. And Dupixent along with the other systemic immunomodulators for atopic dermatitis require prior authorization in all 9 states. And the criteria include some or all of the following conditions: FDA indicated age and diagnosis, documented disease severity, consultation with a specialist, failure with a trial of 1 or more topical or systemic agents.

So, in summary, Clinical guidance for treatment of atopic dermatitis is evolving as evidence for targeted systemic therapies is accumulating. Four systemic immunomodulators have been FDA

approved for treatment of moderate-to-severe atopic dermatitis: Biologics: dupilumab and tralokinumab. Janus Kinase inhibitors: include abrocitinib and upadacitinib. Dupilumab and tralokinumab are FDA indicated when topical therapies are inadequate, and Abrocitinib and upadacitinib are FDA indicated when other systemic drugs, including biologics, are inadequate.

In 2017 dupilumab was defined by expert consensus as a first-line systemic treatment for patients with moderate-to-severe atopic dermatitis that is uncontrolled with topical therapies. Per the “Atopic Dermatitis Yardstick” published in 2018: Stepping up to maintenance treatment with dupilumab is recommended for patients who are symptomatic despite an aggressive course of topical prescription therapies for at least 3 weeks. They do recommend a 3-month therapeutic trial and referral to a specialist. Current FFS clinical criteria for all 4 systemic agents require confirmed diagnosis for FDA-approved or compendia-supported use and step therapy with a trial of a medium or high-potency topical steroid and 1 other topical prescription agent (other than a steroid) for a combined duration of at least 6 months prior.

Considering the clinical guidance, the prior authorization for the recommendation is that consideration should be given for prior authorization for the systemic immunomodulators for atopic dermatitis with the following clinical criteria: FDA-approved or compendia-supported diagnosis and age, documented disease severity, and consultation with a specialist. Modification of the indication-specific step therapy requirements is recommended as follows: A trial with a topical prescription agent for a duration of at least 3 months prior to initiating a biologic systemic immunomodulator and a trial with a topical prescription agent and a trial with another systemic agent for a combined duration of at least 6 months prior to initiating a systemic JAK inhibitor. And that concludes this portion of the review. So, I’ll take any questions.

Tony Merola: Any questions for Linda? Okay, hearing none, before we move onto the glucagon agents, just for clarification, that DOH recommendation based upon Linda’s presentation will be incorporated into the PDP recommendations after executive session. So, I just want to make that point of clarification. You will see a DOH recommended modification to the current clinical criteria that you see here at the bottom of the slide. And if there are no questions about the immunomodulators, I know there was a lot of information there, if there are no questions, we’ll move onto the last PDP or Preferred Drug Program review today which is Glucagon agents, and we’ll send it back to Mina.

Mina Kwon: Just doing a sound check again to make sure everyone can hear me okay.

Tony Merola: Yes, Mina, we can hear you very well.

Mina Kwon: Okay perfect. For the last class we will be reviewing today are the Glucagon agents. So, this is an initial review of the class. So, first we will be doing an overview of hypoglycemia. Hypoglycemia is classified as level 1 which is a glucose level of < 70 mg/dL and  $\geq 54$  mg/dL), level 2 which is a glucose level < 54 mg/dL), or level 3 which is a severe event including altered mental and/or physical status requiring assistance to treat. Hypoglycemia can be reversed through administration of rapid-acting glucose or glucagon. For patients unable or

not willing to consume carbohydrates by mouth, the use of glucagon is indicated for treating hypoglycemia.

So, the mechanism of action for Glucagon and some of the newer brands that Ethan will be discussing today, Gvoke which is glucagon, Zegalogue which is a glucagon, Baqsimi which is glucagon is that the increased blood glucose concentration by activating hepatic glucagon receptors, thereby stimulating glycogen breakdown and release of glucose from the liver. Hepatic stores of glycogen are necessary for glucagon to produce an antihypoglycemic effect.

For indications and usage, all the agents are used to treat severe hypoglycemia. Glucagon also on the label has an indication as a diagnostic aid used during radiological exams to temporarily inhibit movement of the GI tract in adult patients. Gvoke is approved for ages 2 and up. Zegalogue is approved for 6 and up, and Baqsimi is approved for ages 4 years and up.

Dosage, availability, and formulation. The traditional Glucagon and Glucagon emergency kit is available as an injection power for solution. Gvoke is available as a kit which is a vial syringe, it is also available as an auto injector HypoPen and a prefilled syringe. Zegalogue is available as an auto injector and a prefilled syringe and Baqsimi is our nasal powder formulation of Glucagon.

Glucagon class contraindications; pheochromocytomas, insulinoma, and any known hypersensitivity to glucagon or any of the excipients.

The class warnings: Administration may stimulate catecholamine release in patients with pheochromocytoma – Patients with insulinoma may experience a lack of efficacy due to exaggerated insulin release after administration – Hypersensitivity and allergic reactions have been reported including generalized rash, hypotension, and anaphylactic shock with breathing difficulties – Lack of efficacy in patients with decreased hepatic glycogen and these patients should be treated with glucose instead. Specific Drugs: – Gvoke: Includes post marketing reports of Necrolytic Migratory Erythema which is also included in Glucagon package insert and is seen if continuous glucagon infusions administered.

The most common Adverse Drug Reactions with the Glucagon agents with injectables include nausea, vomiting, headache, and injection site reaction. For the nasal formulation, common ADRs include nausea, vomiting, headache, upper respiratory tract irritation, rhinorrhea, nasal discomfort, nasal congestion, cough, nose bleeds, watery eyes, redness of eyes, itchy nose, itchy throat, itchy eyes, and sneezing. For drug interactions – Patients taking beta-blockers may experience a transient increase in blood pressure and pulse. For patients taking indomethacin, they may not experience an increase in blood sugar after glucagon administration and concomitant use with warfarin may increase the anticoagulant effect of the drug.

For specific populations, there data with use in pregnancy but has not found a drug associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. And for pediatric

safety and efficacy established for Gvoke 2 years and up, Zegalogue 6 years and up, Baqsimi 4 years and up, Glucagon infants and up.

There were some comparative studies in this class. Baqsimi was compared with intramuscular glucagon. There were three studies that used primary outcome measures in increase in BG  $\geq$  70 mg/dL or an increase of  $\geq$  20 mg/dL from glucose nadir within 30 minutes after receiving glucagon. And all studies demonstrated non-inferiority of Baqsimi intramuscular Glucagon in reversing insulin induced hypoglycemia. Gvoke was compared with glucagon emergency kit and treatment success was defined as an increase in plasma glucose  $>$  70 mg/dL or a relative increase of  $\geq$  20 mg/dL at 30 minutes after glucagon administration. And the results were non-inferior with a similar tolerability profile.

The American Diabetes Association (ADA) guidelines acknowledge that intranasal glucagon and ready-to-inject glucagon preparations for subQ injection are available in addition to traditional glucagon injection powder requiring reconstitution. No specific glucagon product is identified as being preferred. The ADA 2022 Standards of Medical Care in Diabetes recommends that glucagon should be prescribed for all individuals who are at an increased risk for level 2 hypoglycemia which is again defined as blood glucose  $<$  54 mg/dL or level 3 hypoglycemia, accessible as needed.

So, consistent with initial review, the Glucagon agents would be a new class added to the PDL after this meeting. To recap, we discussed the different Glucagon agents and formulations used for hypoglycemia. The newer branded Glucagon agents have ready to inject subQ preparations, autoinjectors, prefilled syringe, and in addition, a nasal powder compared to the tradition Glucagon injection powder requiring reconstitution. Glucagon has class contraindications with pheochromocytoma, insulinoma or hypersensitivity, and allergic reactions. There are specific injection site reactions with injectable, and nasal adverse reactions with the Baqsimi nasal formulation. For clinical comparative studies within class, Baqsimi was not inferior to intramuscular Glucagon and Gvoke was not inferior to Glucagon emergency kit to increase blood glucose levels within 30 minutes of administration. The ADA does not identify specific glucagon products as preferred and recommends it should be prescribed and accessible for all patients at risk for level 2 or 3 hypoglycemia. And that concludes this class review. I'll take any comments or questions.

Tony Merola: Any questions for Mina? Any questions for any of the clinical information that was presented this morning? Okay, hearing none, I think at this time, we will officially recess for lunch and Executive Session. So, Doug we just have to figure out the timing. It is 10 minutes to 12 right now, I think what we'll do is maybe take allow people to take lunch break and then start Executive Session maybe quarter after 12 and try to be back here by 1:00.

Doug Fish: Yeah, I think that sounds reasonable.

Tony Merola: This is a big agenda, we knew that. we got a late start. I think we're doing good with time, but I think 1:00 back into the public session would be good.

Doug Fish: Yeah, that seems reasonable.

Tony Merola: Okay, so let's work on that time. We are adjourning or recessing to Executive Session. Executive Session will start at quarter after 12:00, we will allow people to take a 20 minute or so lunch break, 20, 25-minute lunch break. So, for DUR support staff and DUR members that are involved in Executive Session, we are going to move outside of the WebEx and we're going to move inside Zoom application and please be inside that Zoom application by quarter after 12:00. Any questions from DUR Board support staff or DUR Board members? Okay, we are going to recess to Executive Session and lunch. Thank you.

Doug Fish: ...the Pharmacy Drug Utilization Review Board Meeting. Thank you for rejoining with us, we appreciate it. There were no official actions taken during Executive Session, and as we said earlier this morning, we have no recusals due to any conflicts. So, that is good. So, for our first order of business before the break we heard from the Preferred Drug Program, now I'm going to ask for a motion to discuss the recommendations related to the Preferred Drug Program. So, do I have a motion from the members and then we'll go and do a count and make sure that we have all of our members here. So, do we first have a motion?

Brock Lape: Sure, I motion.

Doug Fish: So, we have a motion from Brock Lape, and do I have a second? Okay thank you Casey. So, let's just go through and make sure that we do have everybody that we can see on the screen that all the audio is working, and just for recording purposes. So, I think we just heard that was Dr. Quinn right Casey?

Casey Quinn: Doug, you need to speak up a little too, sorry.

Doug Fish: Okay, how is that? Is that better?

Casey Quinn: Yes, it is.

Doug Fish: So, do we have Renante, are you with us? Double check your mute button. We'll go to Asa.

Asa Radix: Hello, yes.

Doug Fish: Great, we hear you clearly, thank you. Joe Chiarella?

Joe Chiarella: Here Doug.

Doug Fish: Great, thank you. Tara Thomas?

Tara Thomas: Good afternoon, I'm here.

Doug Fish: Perfect, we hear you thank you. Debra Wittman?

Debra Wittman: Yes, I'm here, thank you.

Doug Fish: Donna Chiefari?

Donna Chiefari: I'm here, thanks.

Doug Fish: Perfect. Jadwiga Najib?

Jadwiga Najib: Yeah, thank you.

Doug Fish: Thank you. Marla Eglowstein?

Marla Eglowstein: Hello, I'm here.

Doug Fish: Thank you, we hear you good. Casey Quinn.

Casey Quinn: Yep, hi Doug.

Doug Fish: Hi Casey, good. Jill Lavigne?

Jill Lavigne: Yep, I'm here.

Doug Fish: Perfect. Pete Lopatka?

Pete Lopatka: I'm here.

Doug Fish: Good. John Powell?

John Powell: Here.

Doug Fish: Hi, John, thank you. And back to Renante, Renante are you with us?

Tony Merola: Yes, I saw him in chat, I believe I saw him in the chat saying he was logged in...

Doug Fish: He was here but. Okay, I can't see that from here, but you see it. He's logged in but we don't have his audio.

Tony Merola: Renante, can you just check your audio connection for us? Let's try again Renante. Do we have an audio connection with you? He can hear us through the chat, I know he can hear us because he's got the chat functioning. So, he's communicating with us through the chat function.

Doug Fish: Okay.

Tony Merola: Renante, as we go through the voting items, could you just include everyone in that chat feature? Thanks, all panelists, I'm sorry, all panelists in that chat feature.

Doug Fish: Okay, good, I think we're set to go and Tony, so we do have a motion to discuss the recommendations. So, Georgia if you want to pull up those PDP recommendations.

Tony Merola: Sure, so we'll review the Preferred Drug Program recommendations from DOH to the Board for any discussion and vote, and Georgia, if you'll just go to the second slide, this is just our standard clinical criteria that's used for non-preferred drugs. The first preferred drug has

been tried by the patient but has failed to produce desired outcome. The second, the patient has tried the Preferred drug and has experienced unacceptable side effect. The third being, the patient has been stabilized with a non-preferred drug. And then any other clinical indications for non-preferred drug which may include any considerations of medical needs and medical needs for special populations. So, that's the standard clinical criteria. So, I think the next slide we can move right into the drug classes. So, the first drug class that we looked at this morning in terms of new clinical information was the antipsychotics – injectable. Currently Invega Hafyera was a non-preferred status. The recommendation to the Preferred Board is moving Invega Hafyera from non-Preferred to Preferred and that's why it's designated there, if this shows on your screen, it's designated in a green font to represent the change. So, again, one change here is moving Invega Hafyera from non-preferred to Preferred.

Doug Fish: Thank you, Tony. So, do we have any comments, questions, or discussion on the recommendation for the injectable antipsychotic that Tony just reviewed?

Tony Merola: Doug should we just state how we're going to do the vote, and our vote total is 14. I just want to make sure we got the number right. I think our vote total is 14.

Doug Fish: Correct, 14.

Tony Merola: Okay, go right ahead. So, we will be voting by consensus, and we'll vote here for each Preferred Drug Program class. So, when we vote by consensus, what this means is I'll first ask for abstentions, then I'll asked for any opposed, and then, we will either ask for a yes or more likely just by calculation knowing that our total is 14, say that it would pass and be Preferred or recommended for approval. So, for the antipsychotic class for injectables, are there any abstentions from voting from the Board members? Anyone opposed? Checking the chat here, okay, so this passes with 14 approving. Next item.

Tony Merola: Okay, the next class is the antipsychotic second generation. We are not recommending any changes here. Just of note, there is a number of clinical criteria pieces here that we've designed with this DCs and the STs and part of our review is reviewing that clinical criteria. So, we are not recommending any changes to the drug class, and we're not recommending any changes to the clinical criteria. And that was that clinical criteria that Mina had shown on her last couple of slides as we went through the drug classes with her again. I'm not sure if we captured everything on one slide, but those last 2 slides captured the clinical criteria. But again, no changes from Preferred to non-preferred status, no changes to the clinical criteria.

Doug Fish: Any comments, questions, or discussions for the second-generation antipsychotics? Okay. Hearing none, any abstentions? There are no changes here. Any opposed? So, this passes in favor 14. Next class.



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Tony Merola: Next class is the other agents for Attention Deficit Hyperactivity Disorder. Again, we looked at the clinical criteria, no changes to the clinical criteria. And just one change to Preferred non-Preferred status moving clonidine ER from non-preferred to Preferred.

Doug Fish: Thank you Tony. Any comments, questions, or discussions about the Attention Deficit Hyperactivity Disorder class and the addition of a Preferred agent? Nothing in the chat, hearing none, we'll go ahead and vote. Any abstentions? Any opposed? Okay, this passes 14 for Attention Deficit Hyperactivity Disorder recommendation.

Tony Merola: Next class is the Immunomodulators – systemic. So, we are not proposing any changes to Preferred and non-preferred status here, so that's what this slide represents, no changes to the drug classes and their current status. But we do have one change in terms of the clinical criteria that we reviewed, and it resolves around a presentation that Linda Catanzaro did this morning. I believe that's represented on the second slide and I can walk you through that slide. So, this is the information from the PDL itself in the clinical criteria column with some changes. So, you'll see in the atopic dermatitis line item there that we have struck through our current clinical criteria and are recommending new clinical criteria associated with just atopic dermatitis. Everything else stands true with no changes. So, the old criteria that has a strike through there is a trial with a medium or high potency topical steroids AND one other topical prescription agent other than a steroid for a combined duration of at least 6 months prior. So, we're looking to change that to the following clinical criteria that's down at the bottom of this slide. And again, depending on if you can see the different color font here, it's in green font. So, we're proposing to change that clinical criteria for the atopic dermatitis indication to, Trial with a topical prescription product for a duration of at least 3 months. And then for the JAK inhibitors, for the Janus Kinase Inhibitors that fall within the class that are indicated for atopic dermatitis, additional criteria which is, A trial of a topical prescription product and a systemic product for a combined duration of at least 6 months.

Doug Fish: Thank you Tony. Any comments, questions, or discussions about this recommendation? So, again, no changes in the class but change in the indication for the atopic dermatitis that Tony just reviewed. Again, any comments, questions, or discussion before we vote? Hearing none, any abstentions? Any opposed? Okay, this recommendation passes with 14 votes, thank you.

Tony Merola: This was the new class for the Glucagon agents. So, this is a new class. So, I'll just read through the recommendation in terms of Preferred status it would be Glucagon injection, Glucagon HCL emergency kit and in parenthesis there, is the manufacturer. We want to delineate between that particular product and the Glucagon Emergency Kit that's on the non-preferred side, so this is the product that's made by Fresenius, and Zegalogue. So, those are the products recommended to be Preferred status. Non-preferred status is Baqsimi, the other Glucagon Emergency Kit formulation, and Gvoke.

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Doug Fish: Thank you Tony. Any comments, questions, or discussions on the Glucagon agents? And remembering, this is a new class and the non-preferred is still available through prior authorization. I don't see anything in the chat. Once again, any comments or questions, or discussion? Hearing none, we will vote. Anyone who abstains? Any opposed? Nothing in the chat, this passes by 14. I think that concludes the PDP?

Tony Merola: Yes, that concludes the PDP and just for point of clarification, the recommendations have to go to the Commissioner, so the question that always arises is, when will these recommendations or these changes when will they be available? Can't answer that question until they go to Commissioner to get approved. So, that question always comes in. So, again, these will be the recommendations of the DUR Board to the Commissioner for final approval. I think we finished up the Preferred Drug Program part of the agenda.

Doug Fish: Excellent, thank you all for voting, and thank you Tony. So, now up next is a presentation as part of our Drug Utilization Review Items, and the first is aducanumab and Dr. Barb Rogler from SUNY Buffalo. So, Barb you're up.

Barb Rogler: Thanks very much Doug. So, we're going to start today with Aduhelm aducanumab. When I first heard about PAD, all I could think of was peripheral artery disease. But it's Practitioner Administered Drug. So here we go, this is our first one going through this system. The aim of this review is to provide recommendations for the management of aducanumab to the Medicaid program. Aduhelm or aducanumab was approved by the FDA on June 7, 2021.

Now, how I am going to approach this is I'm going to give you this first background slide. As we know, there is a lot of controversy with this product. So, I wanted to first give you the background and then I'll move in and discuss a little bit about what CMS did. So first, the background. This product is FDA approved for Alzheimer's disease. Treatment should be initiated in patients with mild cognitive impairment or as referred into literature as MCI or mild dementia stage of Alzheimer's disease. This product was approved under the FDA accelerated approval process based on surrogate endpoint of reducing amyloid-beta plaques in patients with mild cognitive impairment or mild dementia stage of Alzheimer's disease.

Now, we need to break that apart a little bit. The FDA defines the surrogate endpoint as a marker such as a laboratory measurement, radiographic image, physical sign, or other measure that is thought to predict the clinical benefit. But it is not itself the measure of clinical benefits. And that will become very important as we start to talk about CMS's position. Now, CMS recognizes that this drug was approved under a surrogate marker. And when you're approved in an accelerated approved process, within that approval, the FDA will require the manufacturer to conduct, for this particular one, for aducanumab, the FDA has required that they must conduct a randomized controlled trial confirming the efficacy of Aducanumab compared to an appropriate control for the treatment of Alzheimer's. The final report of the results must be submitted to the FDA by February 2023, in order for the product to remain on the market. The product is a

human immunoglobulin monoclonal antibody designed to promote the clearance of amyloid that aggregate and insoluble forms of beta amyloid in the brain. Amyloid plaques in the brain are a pathophysiological feature of Alzheimer's disease. The pathophysiological hallmarks of Alzheimer's disease include the accumulation of beta amyloid plaques outside the neurons and twisted and tangled proteins inside the brain's neurons. The result is neuronal death and damage to brain tissue. These abnormal protein deposits define Alzheimer's disease. We will talk through this presentation about these biomarkers. This makes Alzheimer's a unique neurodegenerative disease among different disorders that can lead to dementia.

So, now I'm going to change gears just a little bit. We're going to talk about what CMS did and what happened. So, the Centers for Medicare and Medicaid which I'll refer to as CMS going forward has issued a national coverage determination for the monoclonal antibodies directed against amyloid for the treatment of Alzheimer's disease. CMS will cover the monoclonal antibodies directed against amyloid for the treatment of Alzheimer's disease under coverage with evidence development for patients with a clinical diagnosis of mild cognitive impairment due to Alzheimer's or mild Alzheimer's dementia. Both must be confirmed with the prevalence of beta amyloid pathology consistent with Alzheimer's disease. In this national coverage determination, the CMS states that the FDA determinations of drug or biologic demonstrates efficacy from a direct measure of clinical benefit is promising, but it does not meet the statute of reasonable and necessary. Based on that, CMS came back with coverage criteria for these products. The monoclonal antibodies directed against amyloid that are FDA approved for the treatment of Alzheimer's disease based upon evidence of efficacy from a change in a surrogate endpoint, considerable reasonably likely to predict clinical benefit maybe covered in a randomized control trial conducted under an investigational new drug application. Or monoclonal antibodies directed against amyloids that are FDA approved for the treatment of Alzheimer's based upon evidence from a direct measure of clinical benefit may be covered in a CMS proposed comparative study. Study data must be collected in a registration. Aduhelm was FDA approved based on a surrogate endpoint and for Medicare, this is Medicare individuals, per the final coverage determination, Aduhelm is covered through a coverage with evidence development only for Medicare patients enrolled in a qualified study. I want to stop here. That is for Medicare.

Now, we're going to move into this where we're talking into our space, the Medicaid. For Medicaid only individuals, these are people with only Medicaid and not dual eligible, CMS states in their National Coverage Analysis Decision Memo summary that states are required to cover Aduhelm when the drug is used for a medically accepted indication. State Medicaid programs can subject Aduhelm to Utilization Management Techniques such as prior authorization and medical necessity criteria. And that is the reason why we're here today.

Additional background. On the background I goofed it up, I added that slide. On the background, the recommended dose, this drug is a physician administered drug. It is administered via IV infusion. It should be administered every 4 weeks. It requires dose titration to reach a maintenance dose. The dosing is weight based. For monitoring, this is important, the

drug can cause amyloid related imaging abnormalities. We will refer to that as ARIA going forward. It can be ARIA with edema or effusion which is ARIA-E or with microhemorrhages or hemosiderosis which is ARIA-H. Therefore, MRIs are required. One is required 1 year before initiating therapy and before the 6<sup>th</sup>, 7<sup>th</sup>, 9<sup>th</sup> and 12<sup>th</sup> IV infusion. The reason for that is there is enhanced clinical monitoring for ARIA, and it's recommended during those first 8 doses of treatment. If RF is identified in an MRI based on clinical symptoms, severity, dosing may be needed to be descended or permanently discontinued until the MRI demonstrates radiographic resolution and symptoms resolve. Continuation of therapy should be guided by clinical judgment. In patients who develop an intracerebral hemorrhage of great than 1 cm in diameter during treatment, suspend dosing. And again, we'll use clinical judgment to restart treatment or if you're going to continue treatment.

Under the warnings and precautions, we'll talk a lot about patients who are ApoE 4 carriers. So, patients that are ApoE 4 carriers, their status should be considered when initiating treatment for patients. This was really demonstrated in both the EMERGE and the ENGAGE phase 3 trials because patients who were ApoE 4 carriers had a higher incident of ARIA. So, that's what we'll talk about also. Also, in these two studies, the EMERGE and ENGAGE study, these again, are the primary studies that we talk about, patients were excluded if they were using platelets or anticoag therapy other than aspirin less or equal to 325 mg per day. There is little information or data regarding the risk of ARIA in this patient population. Also, in the clinical information, they do talk about the incidence of seizures. There is also the potential for hypersensitivity reaction.

The clinical trials. The first trial, PRIME, this was a phase 1b study, it demonstrated that aducanumab treatment resulted in a dose-and time-dependent reduction in beta amyloid plaques. It was a placebo-controlled period through week 54. There was a long-term extension study to week 518; the extension study was terminated early based on futility analysis of the phase 3 trials. The phase 3 trials were the two identically designed trials ENGAGE and EMERGE. It's unusual for a manufacturer to go from a phase 1b study right to a phase 3 study. So, of the phase 3 studies ENGAGE and EMERGE studies were identically designed phase 3 studies; their objectives were to assess the efficacy and safety of aducanumab in patients with mild cognitive impairment due to Alzheimer's disease and mild dementia associated with Alzheimer's disease. The ENGAGE and EMERGE studies were terminated early based on a prespecified futility analysis conducted by an independent data monitoring committee which indicated the trials were unlikely to reach their primary endpoint. The primary endpoint was defined as to evaluate the efficacy of monthly disease of aducanumab to slow cognitive and functional impairment as measured by changes at week 78 in the clinical dementia rating sum of box force as compared with placebo in participants with early Alzheimer's disease.

I would like to take some time and actually talk about the clinical design of these two phase 3 trials. They were phase 3, these are both the EMERGE and ENGAGE trials. They were a phase 3, multicenter trial, randomized, double-blind placebo-controlled parallel group studies. It is very important that we pay attention to both the inclusion and the exclusion criteria, because

these two bits will lead to how we want to make recommendations to the Board. Patients in these trials were between the ages of 50 and 85 years of age and they must have met all the following clinical criteria for mild cognitive impairment due to Alzheimer's disease or mild dementia related to Alzheimer's disease. They had to have a clinical dementia rating global score of .5. Objective evidence of cognitive impairment at screening. A mini mental state exam, MMSE score between 24 and 30. A positive amyloid PET scan. Consent to ApoE genotyping and a reliable informant or healthcare giver. Also, if they were using other drugs to treat Alzheimer's disease, the symptoms of Alzheimer's such as an anticholinergic, the dose must be stabilized for at least 8 weeks before the screening of the first visit.

Now, the exclusion criteria. Any medical or neurological condition (other than Alzheimer's disease) that might be a contributing cause of the subject's or patient's cognitive impairment. If they had a stroke or transient ischemic attack or TIA, or unexplained loss of consciousness in the past 1 year. Clinically significant psychiatric illness in the past 6 months. History of unstable angina, an MI, advanced chronic heart failure, or clinically significant conduction abnormalities within 1 year before screening. Indication of impaired renal or liver function. HIV infection. Significant systematic illness or infection in the past 30 days. Relevant brain hemorrhage, bleeding disorder, and cerebrovascular abnormalities. Any contraindications to brain MRI or PET scans. Alcohol or substance abuse in the past 1 year and if the patient was taking blood thinners except for aspirin at a very low dose, less than or equal to 325. Quite an extensive list of exclusion criteria for geriatric patients.

Continuing to the next slide for the phase 3 clinical trial study design, if we look at the interventions, patients were randomized to low dose which was 3 mg/kg for those patients that were ApoE 4 carriers and 6 mg/kg for noncarriers. There was a high dose arm which was initially 6 mg/kg for those patients that were ApoE 4 carriers and 10 mg/kg for noncarriers. Later in the trials, the trials were amended and both patient groups were allowed to increase to 10 mg/kg. There was also a placebo arm. Again, patients were allowed to continue other medications to treat their cognitive symptoms if they had been on a stable dose for at least 8 weeks. The primary Outcome was to evaluate the efficacy of the monthly doses of aducanumab in slowing of cognitive and functional impairment as measured at week 78 in the Clinical Dementia Rating Sum of Boxes score as compared to placebo in patients with early Alzheimer's disease. A little bit about the Clinical Dementia Rating Sum of Box scores. .5 indicates questionable impairment predictable of mild cognitive impairment. As the scores increase between 0 to 18, then, the patient's severity of dementia also increases.

Moving onto the results of both the EMERGE and ENGAGE trials. If we look at the age, we can see it's relatively across both studies in all the arms, placebo low and high dose, you'll see that the average age was right around that 70-year mark. You can see that over 50% of the population were female across both studies. You can also see that Alzheimer medication such as anticholinergics were used in about 50% of the population.

Now, moving onto these next two points, ApoE 4 carriers, if we look at the numbers across both studies, you can see its runs right about 67% up to over 71% in different arms of this study. And as you can see, there were much lower numbers of noncarriers. The primary endpoint was achieved in the EMERGE study in the Aduhelm 10 mg/kg high dose study group only, based on the final data set or a later data set. When they first opened it up, they did not notice that. The change in the dementia rating Sum of Box from baseline to week 78 when compared to placebo had declined by .39.

The clinical trials adverse event rates. The instances of adverse events were similar across the groups in both studies. Adverse events were an incidence of greater than 10% in any of the groups were ARIA-E headaches, brain microhemorrhages, also referred to as ARIA-H, nasopharyngitis, falls, localized superficial siderosis and dizziness. The majority of ARIA-E occurred within the first 8 doses and were more often detected in patients who were ApoE 4 carriers and had received the higher dose of aducanumab, so that would be the 10 mg/kg dose. Brain microhemorrhages and localized superficial siderosis were higher in the aducanumab treated participants that had experience in ARIA-E. In the Aducanumab 10 mg/kg study groups of both the EMERGE and ENGAGE studies, the incidents of ARIA both ARIA-E and ARIA-H was 41.3% and in the placebo study group, the incidence was 10.3%. There were no deaths due to ARIA in either study.

Suggested coverage parameters. These are from the American Academy of Neurology Guideline Subcommittee suggests the following criteria for the appropriate use of aducanumab. So, first, it's most important that we identify the person with early Alzheimer's disease which, in order to do that, they suggest a detailed patient history, use of standardized scales and tests to corroborate cognitive decline, Neurological and physical exams, a medication drug list, laboratory testing to exclude other concomitant disorders that can cause cognitive decline, and an MRI to rule out other conditions that can present with cognitive decline. Additionally, there needs to be confirmation of beta amyloid plaque deposits in the brain via amyloid positive PET scan or an analysis of the cerebral spinal fluids. A pretreatment brain MRI is recommended to avoid the administration of drugs in patients with cerebrovascular disease and/or patients with localized superficial siderosis, or greater than 4 microhemorrhages, or a brain hemorrhage greater than 1 cm in diameter. Because of the risk of ARIA, patients who have clotting disorders or are receiving anticoagulant therapy other than low-dose aspirin should not receive the drug treatment. ApoE genotyping should be considered as it may affect the drug's dosing. This whole story is evolving and in a recent update in probably the last 2 weeks, the observation study of Aducanumab in participants with Alzheimer's disease in the US has been terminated as it is expected there will be limited usage of the drug in clinical practice making the study not feasible for enrollment. A Study to evaluate Safety and efficacy of Aducanumab in participants with Alzheimer's Disease who previously participated in the following studies, PRIME which was the 1b study, Phase 2 and phase 3 identically designed studies, ENGAGE and EMERGE and in EMBARK studies will continue. A Study to Verify the clinical benefit of Aducanumab in participants with Early Alzheimer's Disease will begin recruitment. The manufacturer Biogen

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put out the following statement that it would “substantially eliminate its commercial infrastructure supporting Aduhelm, retain minimal resources to manage patient access programs, including to continue a free drug program for patients currently on treatment in the United States”

In summary, aducanumab is FDA approved for the treatment of Alzheimer’s disease. The treatment should be initiated in patients with mild cognitive impairment or mild dementia stage of Alzheimer’s disease, the population in which treatment was indicated in clinical trials. It was approved under the FDA accelerated approval process based on a surrogate endpoint of reducing beta amyloid plaques in people with mild cognitive impairment or mild dementia stage of Alzheimer’s disease. To maintain the approval, the manufacturer must conduct a randomized controlled trial confirming the efficacy of compared to an appropriate control for the treatment of Alzheimer’s disease. CMS encourages state Medicaid programs to subject aducanumab to utilization management techniques, such as PA or medical necessity.

Now, here are our recommendations to the Board. And as I go through the recommendations, I will explain why we made these recommendations. These are the recommendations that are beyond what is in the current package insert. So, the first recommendation, we really want to ensure that this product is being used in the appropriate population. We want evidence existing of mild cognitive impairment due to Alzheimer’s disease or mild Alzheimer's dementia by a Clinical Rating scale such as the Clinical Dementia Rating Scale - Global Scale. We want to look for a score of 0.5 to 1, Mini Mental Status (MMSE) between 24 and 30, and/or a Montreal Cognitive Assessment (MoCA) score of at least 18. So, first, we want to have documentation based upon a validated clinical tool to measure cognitive impairment. That’s why recommendation 1.

Recommendation 2. For those patients, we also want to know if the patient is an Apolipoprotein 4 carrier status. As we saw in clinical trials, those patients who were carriers ApoE 4 carriers had a higher instance of ARIA and we saw more ARIA at the higher doses. So, this could actually, if a practitioner did know a patient’s status, this could guide their dosing for that patient.

The third recommendation. A positive PET scan or positive CSF analysis was completed that was positive for amyloid beta deposits. Because we know the mechanism of this product, what it does is reduce beta amyloid deposits in the brain. So, we need to confirm that this patient actually does have beta amyloid based on the results of these scans or else an analysis with CHF that they do have beta amyloids.

Again, question 4, the next criteria really goes to identifying that appropriate patient. The patient does not have evidence of any medical or neurological condition other than Alzheimer’s disease that might be a contributing cause of the subject's cognitive impairment. And there is a whole list, but we did leave some here for you. Also, based on the exclusion criteria in the clinical trials, the patient does not have a history of clotting disorder or is not taking any form of

antiplatelet or anticoag medication other than low dose aspirin. And finally, again when we wrote the policy, it would be consistent with the FDA approved product information. I will take any questions that the Board has now. Thank you.

Doug Fish: Thank you Barb. So, comments, questions from the Board regarding Barb's presentation.

Jill Lavigne: I don't have a question about the presentation, but I am wondering if it's possible for New York State Medicaid to have a policy similar to Medicare or if we're limited by federal laws to have a more generous policy?

Barb Rogler: In that memo we do have to cover the drug. And the reason we have to cover the drug is under statute. They participate in the federal rebate system. So, we have to have a lot of access to this product. And so, that is why we will not be able to cover it under a randomized control trial is because we need to allow access to the product because they participate in the federal rebate program.

Jill Lavigne: Alright thank you.

Doug Fish: That was a very good question though and it's come up so, thank you for asking that. And I'll just mentioned that these recommendations here are UB's recommendations to the Department as we'll hear later about the Department's recommendations. But other comments, questions, or discussion?

Joe Chiarella: Hi, it's Joe Chiarella. I thought I heard at the beginning a requirement that this would not go through something like a prior audit or review in a managed care plan. Are there criteria besides that? I mean, can somebody just send a prescription and expect it to be covered and paid without review?

Barb Rogler: Let me rephrase your questions so I make sure I understand your question. I must say this, under New York State Medicaid would be covered, because its physician administered, under a medical benefit right. so, this claim would not adjudicate at the point of service in a pharmacy environment. It would have to, it's a retrospective review of this product. So, it is a medical benefit. But if I hear you correctly and from past experience, what would happen in managed care is they would put this under a medical necessity right? So, in managed care, they would be allowed because they could say, okay this product needs to be reviewed as medical necessity before a patient can be prescribed this drug, we need to ensure that the patient has mild cognitive impairment and meets all the criteria of that managed care plan. Managed care plan will probably put out a policy. From the Medicaid perspective though, because we're going through the physician administered program and we are a medical benefit, we are doing this retrospective. We are developing a policy for the management of Aduhelm within our program. And that's what we are doing here. It would be slightly different than what you would see in the commercial markets or if you had a part D program or Medicare program.



Kim Leonard: This is Kim Leonard, just to clarify with these medications, the expectation at least for a Medicaid managed care plan would be that whatever criteria we have that their approval is not more stringent?

Doug Fish: Joe, does that answer your question?

Joe Chiarelli: Yeah, I think so, thank you.

Doug Fish: Thank you. Other questions? This one is complicated. Any other comments, questions, or discussions? Okay. Hearing none, do I have a motion to go to the Department's recommendations? Anybody want to motion?

Brock Lape: This is Brock, I'll motion.

Pete Lopatka: This is Pete I'll motion.

Jill Lavigne: And I'll second it.

Doug Fish: I appreciate that. So, I'll turn it over to Tony.

Tony Merola: Okay. So, there's a number of recommendations that are mirrored after what Barb just presented. So, I will walk you through them. I'll walk you through them through the entire several recommendations, then we can backtrack and discuss and vote after at least we show them so we can get the full picture. So, Georgia if you just move the second slide here. It's just a point of clarification that the coverage policy as we've described it on the pharmacy benefit side is the coverage criteria, the coverage policy will confirm. FDA approved use in accordance with FDA package labeling or compendia-supported use. So, we just wanted to make a point of clarification there. That's not the recommendation, its just a point of clarification. The following are the recommendations based upon the review we had just done or Barb has just done of currently available drug information guideline and any drug utilization review that we might have on this product or any of the products we look at or review later on today. So, that's the first slide, but there come the recommendations.

So, very similar to what Barb has just presented. Before initiating aducanumab or Aduhelm, prescribers must attest the patient is diagnosed with mild cognitive impairment due to Alzheimer's disease or mild Alzheimer's dementia by meeting one of the following. So, by meeting one of the following: The Clinical Dementia Rating Global Score of 0.5 to 1. Mini-Mental Status Exam Score between 24 and 30, and the Montreal Cognitive Assessment score of at least 18. That's number one.

We'll move onto number 2. Before initiating aducanumab (Aduhelm) prescribers must attest that the patient has undergone the following pretreatment testing, genetic testing to assess apolipoprotein E 4 ApoE 4 carrier status and positron emission tomography (PET) scan or cerebral spinal fluid analysis to confirm the presence of amyloid beta deposits.

The next one, before initiating aducanumab or Aduhelm, prescribers must attest the patient does not have any evidence of medical or neurological condition other than Alzheimer's disease that could be contributing to the patient's cognitive impairment.

I think we have one more. And the last recommendation, before initiating aducanumab (Aduhelm), prescribers must attest the patient does not have a history of a clotting disorder and is not taking any form of antiplatelet or anticoagulant medication other than aspirin equal to or less than 325 mg/day.

Doug we can go back to the first recommendation to see if there is any discussion or conversation around it. Do you want to do that?

Doug Fish: Let's go to the top yes, and we'll take these individually I believe right?

Tony Merola: Okay so we're going to the recommendations. I'll read them again just for clarity. Please bear with me as I get through a lot of text here. Recommendation 1 - Before initiating aducanumab Aduhelm, prescribers must attest the patient is diagnosed with mild cognitive impairment due to Alzheimer's disease or mild Alzheimer's dementia by meeting one of the following: The Clinical Dementia Rating Global Score of 0.5 to 1. Mini-Mental Status Exam score between 24 and 30, and the Montreal Cognitive Assessment score of at least 18.

Doug Fish: Thank you Tony. So, any comments, questions or discussion regarding recommendation 1? And basically, what these screening criteria are, these scores are in the range of mild cognitive impairment.

Tara Thomas: Doug and Tony, this is Tara. I'm trying to move out of the managed care space and over to the Medicaid fee for service to understand how this works. So, I know we had the presentation this morning about PADs and kind of the future vision that the Board would see for how to redo these and recommend criteria. But in the Medicaid fee for service space, are providers needing a prior authorization before initiating treatment? Because I heard Barb say a couple of times, that these are retrospective reviews. So, I just want it clear in my head as to like when you're seeing this criteria. Is it before initiation or has therapy already started and you're looking at the claim?

Barb Rogler: Tara thank you very much for the question. We are actually looking at these claims' retrospective right. It's not that they require a PA. At the point we are with implementation of this program based on the presentation this morning, we are not at the point of doing a prior authorization. This is retrospective after the dose has been given and then we go from there.

Monica Toohey: Hey Tara and actually you know it's not, we were doing this presentation first before we actually opened up the product for processing officially with the actual codes. So, I mean as far as they are reviewed, its just that its reviewed kind of after but we still want to post all the criteria and as we move forward to the new process, we would like to get that done up front, just like we do for regular pharmacy plans.

Tara Thomas: So, I didn't hear all of that.

Kim Leonard: Hi Tara, it's Kim. So, I think what Monica said was that the criteria is going to be made available for prescribers on our website. We have a website that went up, well actually a little while ago but we've done a lot of work to improve that and that's kind of our first step in implementation of some of these requirements prior to getting a more retrospective review. So, the drug information will be posted and available and there will also be worksheets that are submitted with the claim which walks the practitioner through all of the requirements for coverage.

Tara Thomas: Is there any consideration given the fact that this is retrospective, sorry I'm having a hard time separating myself again from the managed care space, around like specialists making sure that it's being administered by a neurologist or that, so with each claim and worksheet, would you be evaluating these markers and the different scores and stuff?

Kim Leonard: Yes, so each individual claim in that case goes through an individual manual review.

Tara Thomas: Okay.

Kim Leonard: So, unlike pharmacy where a lot of that is done systematically, we're able to, as the claim comes in, evaluate medical history and prior diagnosis and sometimes even laboratory testing. This is all done within the claim's submission. So, they're going to have to submit this documentation to us.

Monica Toohey: Yeah, like Kim was saying with the worksheet, it will have this laid out. If you've seen some of the other worksheets that we've done now on that website, we kind of put in all those different, whether they have to check it off, they have to add the information. So, the expectation that they follow these rules, it's just that we don't have currently in the structure that up front kind of block. So, we're expecting that they follow the rules. When they do the retrospective pending review, they're going to look to see all these things have been completed.

Tara Thomas: Okay, thank you.

Joe Chiarelli: It's Joe Chiarelli if I could ask, you're saying that you're going to check to see that everything's completed, but it looks like they only have to, the prescriber only has to send in an attestation. Again, I'll try and separate from managed care role, but attestations don't always match up to the records that you eventually see.

Monica: Well, the expectation is that they would and upon audit that you would see that all that is completed. And then, you know, again, once we move to the more robust system, you're going to have a lot more of that upfront and confirmed. But for right now, that's the best we can do to start, and it is a current process that is utilized as we try to move out of it. But yeah, it's the expectation that it's being done. That's why it's being published and communicated.

John Powell: This is John Powell; I hate to interrupt Doug and Tony. As this week we previously discussed, I'm going to have to excuse myself in a couple of minutes from the meeting, but I am glad to see you still have a quorum, so my apologies for that and thank you.

Doug Fish: Thank you John, we understand.

Kim Leonard: So, for recommendation number 1, too, I think prescribers must attest, that is the recommendation back in OAC modified based on a recommendation from the Board. If submission of that information is deemed more appropriate, then that is something that could be requested or recommended.

Doug Fish: And there's a couple of questions in the chat that one, wondering if Board trained and certified geriatricians could administer this in their office?

Barb Rogler: We are not limiting this drug to any specialist. So, absolutely, if a board trained geriatrician wanted to administer this product in their office, they had access to the appropriate medication, appropriate IV pump, appropriate emergency responses and things like that, then absolutely, yes. We did not put a portion in here about limiting the use of this product to any specialist.

Doug Fish: Thank you Barb and another question relates to the score on the Mini-Mental Status Exam. This says between 24 and 30 and I think 30 is the total. So, 30 is normal, so why is that included, and do we have the right range here?

Barb Rogler: Yes, that is what was included in the clinical trials and the inclusion trials. This is from Ignacio right those questions. I understand because he's in the nursing home and he's not seeing patients when they get to the nursing home with a Mini-Mental score of that. He's seeing those patients, and I don't mean to be putting words in his mouth, but since he can only chat, he's seeing patients with scores you know, well below 24. He's seeing in that 10 range, things like his patients who are severely impaired. So, I totally hear what he's saying, but that was what the inclusion criteria in the study, so we went with the inclusion criteria of the study.

Doug Fish: Okay, thank you. Other questions? Okay, hearing none are we ready to move to a vote on this recommendation? Renante just also mentioned the 25 to 30 is typically normal in geriatrics in general but we can certainly verify that this is the scoring for the study that this is where we took it from. The clinical trial criteria correct, Barb?

Barb Rogler: Yes, we took it right from the clinical criteria from the trials and again, we're looking at patients with mild cognitive impairment. We're not looking, so these are patients that are still functioning, and even when they talk about the EMERGE trial they talk about the ENGAGE trial, they're talking about people still at home, still functioning, and have mild cognitive impairment. And his point is well taken because it's a fine line with identifying these patients with mild cognitive impairment, and we're doing it off a validated scale, right. And I understand his concern with this, but again, this was how they identified patients in the clinical

trials, and one could suggest that maybe it was too high, and the range is too tight. But this is just one of the tools that they used. But they did use the others too.

Doug Fish: Right. So, if they were concerned about that then yeah, a different rating scale could be used. Okay. Any other comments or questions? Okay. So, I think we'll move forward for a vote here. Again, we'll vote by consensus, so I'll first ask for abstentions, then any opposed and then those in favor. So, do we have anyone abstaining from voting on aducanumab or Aduhelm this first recommendation about the clinical screening criteria for mild cognitive impairment? Any opposed? In the chat here, okay so this first recommendation passes 13 members noting that John Powell is no longer with us for this portion of the meeting. Okay Tony let's go to recommendation number 2 please.

Tony Merola: Sure, before initiating aducanumab (Aduhelm) prescribers must attest that the patient has undergone the following pretreatment testing, genetic testing to assess apolipoprotein E 4 carrier status and positron emission tomography (PET) scan or cerebral spinal fluid analysis to confirm the presence of amyloid beta deposits.

Doug Fish: Thank you, Tony. Any comments, questions, or discussions on this recommendation, pretreatment testing? for both determination of carrier status and then either a PET scan or CSF analysis for an amyloid beta deposits.

Joe Chiarelli: Again, it's Joe. I guess my question is, if we think we might have claims on file and we might have results certainly of the scans, do we want to ask for the actual medical records rather than an attestation?

Monica Toohey: Yeah, you can definitely make a recommendation to do that. I think just because of the way we currently do things today, it made more sense to write it that way for us but you can certainly change the recommendations to say the values have to be provided. I mean, if they're attesting that its done, they should have values, so to me its kind of almost means the same thing. You can make a motion.

Joe Chiarelli: Are we at that spot yet? You are all hard to hear, I apologize.

Doug Fish: Yeah, no, this would be the place to if you wanted to state a motion Joe that you could do that and then we could discuss that motion.

Joe Chiarelli: Okay, I'll go out on the limb here, I'll move that we substitute the attestation for the actual tests, the genetic testing, and the position emission tomography test.

Doug Fish: Do I have a second for the motion to discuss this?

Debra Wittman: This is Debra Wittman, I second the motion.

Doug Fish: Thank you, Debra. Okay, so up for discussion is to revise the recommendation from attesting to providing the actual test results.

Kim Leonard: Doug, I just have a question, since this motion and we're on the second recommendation, is this going to be considered also for the first recommendation too that it's the actual results or I'm just trying to remember what the first one was.

Doug Fish: The first one was just the score.

Kim Leonard: Oh, alright.

Doug Fish: I think we're just talking about this recommendation now of the test result itself, making sure that they would...

Joe Chiarelli: Yeah, that's what I meant by just this motion would apply to recommendation number 2 in the screen right now.

Donna Chiefari: This is Donna, I just have a question about this. Since it's a retrospective review, if we were to find that the practitioner who administered the dose but did not have this documentation, what happens?

Kim Leonard: I mean it's a little bit different process than the pharmacy area and there is a little bit of back and forth that goes along with that, but I think the provider is at risk for not being reimbursed.

Donna Chiefari: Okay, thank you.

Tony Merola: I think we're going to try and make a real time change here Georgia I trying to capture the motion by Joe.

Doug Fish: It could just say provide documentation or did you offer wording Tony?

Tony Merola: Yeah, we're working on the wording now that they must provide the values.

Barb Rogler: I don't think he wants the word values on there I think what he wants is the actual medical chart with the scans. So, we have to be very specific that we want the medical, the physical laboratory results and documentations that the test occurred. We do not want it in progress notes, we want the medical record.

Doug Fish: So, Georgia has provided wording here. Joe, does this meet, I'll read it now, Before initiating aducanumab (Aduhelm) prescribers must provide the results for the following pretreatment testing. So, replacing attest with muse provide the results.

Joe Chiarelli: So, my comment on this one Doug would be there's a difference between providing the results, I could scribble it on the back of an envelop as opposed to providing the medical records documenting the pretreatment testing.

Doug Fish: What wording would you suggest?

Joe Chiarelli: How about medical records instead of results.

Doug Fish: Okay. So, now it reads: Before initiating aducanumab (Aduhelm) prescribers must provide the medical records for the following pretreatment testing. This is the apolipoprotein E epsilon 4 carrier status and PET or CSF amyloid beta deposit results. Further comments or discussion on this revised recommendation? Okay. Are we ready to move to a vote? Anyone who abstains? Any opposed? And again, now it reads: Before initiating aducanumab (Aduhelm) prescribers must provide the medical records for the following pretreatment testing. Any opposed? Hearing none, this passes 13 approved. Okay recommendation number 3.

Tony Merola: Okay, before initiating aducanumab, prescribers must attest that the patient does not have evidence of any medical or neurological condition other than Alzheimer's disease that could be contributing to the patient's cognitive impairment.

Doug Fish: Thank you, Tony. Comments, questions, or discussions on this recommendation?

Tara Thomas: Hi, it's Tara again. I noticed that at least the first story I don't remember if the fourth one has the same wording, but they all start with: Before initiating. So, I feel like the criteria only applies to the first claim that you get for a member. How will subsequent claims be reviewed? Sorry, if that's a big question.

Barb Rogler: No, Tara, it's not a big questions, it a very appropriate question. Because you're right with initiating, but when it's required for renewal, we're still going to have to see those Mini-Mental scores hold or improved and not declined. Whatever your validated tool that you used at baseline, we're either going to have to see an improvement of them or stabilization of those scores. And then the other part that we're going to have to see are that the MRIs were also completed during that first 8 doses. So, those will be the big things that we will want to see. like for this one, since you're getting the medical records and you already see the beta amyloid plaques and things like that in the PET scans, and we know that the hallmarks of the biomarkers of Alzheimer's disease are beta amyloid plaques and \_\_\_\_ proteins and this may be one of those areas where, you know, because you've already got the medical record, you're just having the provider attest. But I hear what you're saying on the renewal. Because we would have to look on the renewal for either like I said the validated scores from the baseline using the same tool, completion of the MRI without ARIA-E or H, things like that. So, you're right, we are remiss in...

Tara Thomas: And we need a recommendation number 5 then to include if we're posting criteria for providers to refer to?

Barb Rogler: I think so, yes. I apologize that we were remiss in not doing that. So, do you want me to write it?

Doug Fish: Sure, or we can, go ahead Joe.

Joe Chiarelli: Let me just see if...

Tara Thomas: yes, we can do that when we get through the 4 recommendations. I didn't mean to move the focus.

Joe Chiarelli: Okay but again, the point I think was it says before initiating. Someone submits a claim, I mean given the cost are they going to submit a claim after every dose? Are they going to submit a claim after the 8 doses? I haven't read anything that says how long the approval period was be for, and how often we would expect to see the documentation.

Monica Toohey: This is Monica. I think that can vary on some of the different criteria's that we've done but these are done on a per claim basis. That said, it doesn't mean that if they review an initial and then when they're doing, they realize as they're reviewing subsequent ones that they're just reviewing certain subsets again to make sure there's improvement, you can do that. But in the current way that we review it, it is on a per claim basis. So, it's not really the PA is good for like in pharmacy it could be good for a year or whatever. There could be reviews at different stages of the claim.

Joe Chiarelli: So, if our documentation, our slide up here says, before initiating, are we contenting to say before initiating and during treatment?

Monica Toohey: We could do that but I don't know that every single component would need to be provided for the subsequent. So, on some of the ones that we've done that are like historical that we have on our website, we have the initial and then for the subsequent we just looked for particular pieces of the criteria to validate that it was still working, and they were still getting clinical facts, or if they were still utilizing some kind of medication concurrently with it. Like that still was validated. So, we could put a slide together that either we can try to incorporate it into these but I think it just might be easier as a separate slide to say for subsequent or continuation of therapy, these things have to still be validated per claim.

Joe Chiarelli: Sorry, I agree with that 100% because otherwise, someone could just write on the third claim, continuation of therapy, this is not before initiating, so it is good to spell it out. So, I would agree with that, thank you.

Doug Fish: And thanks for raising it Joe and Tara. And so, Monica if it's an every 4 week administration anyway, right? So, the way that the trial was done it was like before the 6<sup>th</sup> dose and they prescribe out when those monitoring things should occur.

Monica Toohey: Yeah, we can get to that level when we create the worksheet criteria and that's how we did it on a lot of the ones that we already have that didn't necessarily go through this process, but we had as a policy. And I think we could try to kind of remember this. This is new for us coming out here, doing some of these here up front so we can try to remember that going forward that we can think about initial and then think about the continuation.

Doug Fish: Thank you. These are all good comments making us think here.



Monica Toohey: Well, it is because I think about pharmacy, the other thing we do and whenever we do like a step therapy and different things, we automatically do initial right and then as people are stabilized, we take that into consideration and we only look for certain things after. But on this, because it is a little bit more detailed in how we're writing this out, we do need to think about that.

I think we have one more. And the last recommendation, before initiating aducanumab (Aduhelm), prescribers must attest the patient does not have a history of a clotting disorder and is not taking any form of antiplatelet or anticoagulant medication other than aspirin equal to or less than 325 mg/day.

Doug Fish: So, back to recommendation number 3, so this is really the initial dose back to Tara's question. So, before initiating aducanumab or Aduhelm, prescribers must attest that the patient does not have any evidence of medical or neurological condition other than Alzheimer's disease that could be contributing to the patient's cognitive impairment. Any further discussion? Okay. If not, then I think we're ready to vote on this recommendation number 3. Are there any abstentions? Any opposed? Okay, this moves in favor of the recommendation 13 was the count. And recommendation number 4, Tony.

Tony Merola: Okay, before initiating aducanumab, prescribers must attest that the patient does not have a history of a clotting disorder and is not taking any form of antiplatelet or anticoagulation medications other than aspirin equal to or less than 325 mg/day.

Doug Fish: Thank you. Comments, discussion, or questions on this recommendation? And I think again, this just came out of the trial data in this package insert. Any comments? If not, Tony do you have a comment?

Tony Merola: No, we are working on another recommendation over here Doug so, let's finish up with this one.

Doug Fish: Alright. So, I think we're ready to then vote, any abstentions on recommendation number 4? Any opposed? I don't see anything in the chat either, so this passes favorably 13. And the team is working on a fifth recommendation regarding continuation therapy. So, just give us a moment if you could, please. Make sure we have our wording correct.

Tony Merola: So, we just created a recommendation 5 based upon the previous conversations of continuation of therapy. We will put it up here on the projector and we'll walk through it. So, what we've just put together very quickly here is: For continuation of therapy, providers must attest that utilizing the same baseline assessment tool, hold on let me back up here. For continuation of therapy, providers must attest that utilizing the same baseline assessment tool, so utilizing the same baseline assessment tool, that the patients score has remained stable or improved.

Doug Fish: We don't quite have that right, commas in the right place but the gist of it is that the patients score has remained stable or improved. And we're talking about the Cognitive Impairment Screening test. So, we should probably state that.

Monica Toohey: Or you can refer to like within recommendation 1 the test, the records, just try to make it easier.

Tony Merola: So, I'm going to try to paraphrase this so: For continuation of therapy, providers must attest that the patient's, let me go back to recommendation 1.

Doug Fish: So, it's the three scores, it's the Clinical Dementia Rating Global Score or the Mini-Mental Status Exam or the Montreal Cognitive Assessment score. So, all of these are basically the cognitive screening scores. I think it could read, Georgia if we could just kind of change maybe the order: For continuation of therapy, providers must attest that the patient's score remains stable or improved, utilizing the same baseline assessment tool as outlined in recommendation 1.

Tony Merola: Thanks Doug, that was kind of yeah, getting my mind confused.

Doug Fish: And a comma after continuation of therapy as opposed to a semi colon. Okay, so I think, Joe is this and Tara I think are hopefully getting it where we want it to be. For continuation of therapy, providers must attest that the patient's score remains stable or improved, utilizing the same baseline assessment tool as outlined in recommendation 1. Comments, questions, discussions?

Joe Chiarelli: It's Joe again, I don't mean to drag this out, but I am no expert on Alzheimer's or Aduhelm but is documentation that the PET scan changed or got better required in the package insert? And if yes, should we put it here too?

Doug Fish: So, part of that is the MRI, there are recommendations around MRI screening at certain infusion intervals. And Barb reviewed that as part of the background for the recommendations. I think if we get into that level of detail, we would have to kind of bring that back if we were going to go much deeper probably than this in a recommendation. But it's a reasonable point. At a minimum, you would want this. At other time points, there would be other assessments that would be done along the way. So, I think it's true Joe what you're saying. Some of these evaluations are part of the approval process from the FDA. So, it was an MRI within 1 year before starting therapy and then before the 6<sup>th</sup>, 7<sup>th</sup>, 9<sup>th</sup>, and 12<sup>th</sup> infusions, that's how the studies were set up.

Monica Toohey: Hey Doug, I think with the first slide that we're going to follow the FDA labeling, I think we could kind of use that to follow when the MRIs are due, even though its not an official like spelling all those pieces out, we can pull it from there and use it in our criteria. So, by following the FDA labeling, we would make sure at those points we would check the MRI that we could have a check point during the therapy at wherever point they are. Does that make sense, just to make it easier?

Doug Fish: Yes, but you're referring to recommendation 1 and saying...

Monica Toohey: the one that, well the overall recommendation around do we have like a step slide...

Doug Fish: no

Monica Toohey: as we follow FDA? So, it's not actually, I mean we always do this, so because we always do this, it's kind of baked in.

Doug Fish: Okay, so this is always a recommendation.

Monica Toohey: Exactly, and then we'll just make sure when we do like our criteria worksheets, we hit those spots where we're capturing that information.

Doug Fish: Perfect. Okay, very good.

Joe Chiarelli: So, do you think then you don't need to state let's say on the 5<sup>th</sup> slide that the coverage will continue to affirm or, you're okay with just this one? I'm fine with it either way, I don't want to muck it up.

Doug Fish: I think it's a valid point. I think it's good to have the 5<sup>th</sup>, it means that we thought about it, you thought about it. You brought it to our attention and so, that and other things. But I like it. Monica.

Monica Toohey: So, its saying on that slide for the continuation that we would also just kind of reiterate the FDA piece or that we didn't think we needed it? I'm sorry.

Doug Fish: No, I think that's already implied in the baseline, so I think this can stand as it is.

Monica Toohey: That's what I was, yep, sorry.

Doug Fish: So, implied inherent in the process is what you're recommending. This additional recommendation is the attestation that the score is not declining. Other comments or discussion before moving to a vote? There's a comment in the chat. So, this is actually the MMSE and I guess declining, stable, or improved, there is going to be some toggle right within you know it might change by a number or two, but that doesn't necessarily mean it's a significant change, especially as Renante is pointing out, if they use the Mini-Mental Status exam, the results might be skewed if such would expect to go down in the normal aging process in addition. But that would be over years probably not over the 4 to 6, 8, 12, 16 weeks of infusions I presume. So, this would probably be in 6- or 12-month increments is the normal aging process would impact those scores presumably. It's good to kind of keep that in mind that over time, I think mine's already dropped. Okay, hearing no other discussions, and thank you for helping us to put this recommendation together, are there any abstentions? Any opposed? Okay, this passes favorably 13. Thank you all for helping us do that, very good.

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So, that completes the recommendations and the presentation for aducanumab. We have three other presentations, and I don't think I reviewed all those topics up front. There's Botulinum Toxins, infliximab and then vedolizumab. So, next up is Botulinum Toxins right Tony?

Tony Merola: Yeah, that would be the next one up. Our presenter is Holly Coe and Holly is remoting in so, Holly can we just do an audio check with you again?

Holly Coe. Yeah, hi, can you hear me?

Tony Merola: Yep, we hear you loud and clear.

Holly Coe: Okay, I do hear some whispering still on your end.

Tony Merola: We're going to try and resolve that when you start your presentation. So, why don't you get started and hopefully when we hit the mute button on our end, that little background buzz goes away.

Holly Coe: Alright, perfect. Okay, so switching gears a bit here. As mentioned, I'll be reviewing the Botulinum Toxins for the Board today.

Okay, so the primary objective here today is to develop clinical criteria for botulinum toxins for members in the New York State Medicaid program. And utilization will be reviewed for these toxins across the entire NYS Medicaid population, including the fee-for-service and managed care programs.

So, in terms of some background regarding these products, they are neuromuscular blocking agents, and they inhibit the release of acetylcholine. There are four products covered by the New York State Medicaid fee-for-service program and these include AbobotulinumtoxinA (Dysport) – IncobotulinumtoxinA (Xeomin) – OnabotulinumtoxinA (Botox) – RimabotulinumtoxinB (Myobloc). So, all these agents are physician administered.

So, there are multiple covered indications for these products that are approved by the Food and Drug Administration. The indications vary depending on the specific botulinum product. Unless otherwise noted in the table, these products are indicated for adult patients. I also want to mention that this table only includes covered indications by the New York State fee-for-service programs. So, it does not include medications for cosmetic purposes. So, for example, for treatment of glabellar lines, otherwise wrinkles, does not cover for those types of indications. So, there are a total of 10 covered indications, and I will just review them here. Axillary hyperhidrosis or AH, blepharospasms, cervical dystonia CD, chronic migraines as listed for prophylaxis and PI notes this is for patients with chronic migraines who have 15 or more headache days per month lasting more than 4 hours. Other indications include chronic sialorrhea CS, neurogenic detrusor overactivity NDO, overactive bladder OAB, spasticity, strabismus, and then finally urinary incontinence or UI. On the Botulinum Toxin Botox does have most of the approved indications and according to the labeling for this product, I just want to draw your attention, there's a few indications where botulinum toxin is not first line. So, for example for

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axillary hyperhidrosis, it's actually recommended that topical agents prior to Onabotulinumtoxin. And then for the bladder types of indications, specifically NDO, OAB and UI, the labeling does not for this product that patients who are intolerant or not responding to an anticholinergic agent should then attempt OnabotulinumtoxinA. So, in that case it would not be a first line.

So, the next slide summarized the guideline and consensus expert statement recommendations for all of the ten covered indications. So, basically, it's reviewing the placement therapy. For most of the indications, the botulinum toxins are not considered first line, and I will review these as we go along.

So, first for axillary hyperhidrosis, again OnabotulinumtoxinA is only the product for this indication. In terms of first line treatment the expert opinion recommends a topical agent specifically 20% aluminum chloride as first line for most cases. OnabotulinumtoxinA can also be considered. The opinion also notes that if the treatments are not successful, combination treatment may also be considered. And then if those are not successful, oral anticholinergics may also be considered. And then in terms of remaining treatment options, I just briefly, there are other options including microwave therapy, local surgery, or sympathetic denervation.

The next indication Blepharospasm – there are two products listed on the slide with that indication. In this case the botulinum toxins are considered first line so the American Academy of Neurology Guideline in 2016 asserts that the two products are probably effective and should be considered for treating the condition. And this is considered a level B recommendation. They noted that the products are considered to be first line by specialists and have equivalent efficacy. Another product incobotulinumtoxinA is also considered possibly effective and may be considered and this is a level D recommendation however this product is not FDA approved for treating this condition but does have a compendia-supported view. And then the National Institute of Health National Eye Institute does recommend OnabotulinumtoxinA injections and surgery is recommended if the injections are not successful.

For cervical dystonia all four of the covered products have this indication. The botulinum toxins are first line. So, again the AAN guidelines in 2016 asserts that both abobotulinumtoxinA and rimabotulinumtoxinB are considered effective and should be offered for treatment. This is a level A recommendation and in terms of OnabotulinumtoxinA and incobotulinumtoxinA, these are considered probably effective and should also be considered. And that's a level B recommendation.

And then in older guidelines from the European Federation of Neurological Societies in 2011, they do recommend OnabotulinumtoxinA as first line for this condition and they also suggest pallidal deep brain stimulation as another treatment option.

So, for the chronic sialorrhea or hypersalivation indications are two products are approved for this as noted on this slide. There were no American guidelines identified for this indication. However, a National German guideline was identified and they do recommend that glycopyrrolate is recommended as first line for children, adolescents, and adult patients who are in palliative care. the botulinum toxin and it only addresses the incobotulinumtoxin not the rimabotulinumtoxinB products. So, the botulinum

toxins are considered to be an alternative treatment. However, for treating patients with Parkinson's and other nerve degenerative diseases, the botulinum toxins are considered to be first line.

Moving onto migraine prevention in chronic migraine there is only one product indicated for this indication and that the OnabotulinumtoxinA. The American Headache Society issued a consensus statement in 2021 which did assert that the OnabotulinumtoxinA has established efficacy for preventing migraines. They did actually in this consensus statement actually was more focused on integrating new migraine treatments, so for example, the CGRP receptor antagonist. The consensus statement was more focused on these types of products however they do make recommendations concerning patients with chronic migraines. So, they used the International Classification of Headache Disorders third edition to assign chronic migraine as 15 or more headache days per month lasting for more than 3 months. So, they recommend an 8-week trial of two or more of the following topiramate, valproex sodium/valproate sodium, beta-blocker and there are several listed there, a tricyclic antidepressant and a serotonin norepinephrine reuptake inhibitor venlafaxine or duloxetine or an inability to tolerate or inadequate response to a minimum of 2 quarterly injections of onabotulinumtoxinA prior to using a CGRP antagonist.

The Nation Institute for Health and Care Excellent in 2021 issued guidelines and her assert that onabotulinumtoxinA is recommended for patients with chronic migraines who had no responded to at least 3 previous preventive pharmacologic treatments. So, they give examples including topiramate, propranolol, and amitriptyline.

And then an older guideline from the American Academy of Neurology in 2016 recommends use of onabotulinumtoxinA for treatment of chronic migraines as it is considered safe, effective, and may improve quality of life.

So for treatment of overactive bladder and NDO, onabotulinumtoxinA is the only botulinum toxin indicated for those conditions. The American Urology Association and Society of Urodynamics in 2019 issued guidelines that asserted that onabotulinumtoxinA may be offered as a third-line treatment option for patients who have non-neurogenic OAB and who are refractory to first- and second-line treatments. First-line treatment consists of behavioral therapy including bladder training while second-line treatments include antimuscarinics or beta-3-adrenoceptor agonists. NDO, the European Association of Neurology in 2016 guidelines they recommend antimuscarinics such as oxybutynin, trospium, tolterodine as first line treatment of NDO. They do note however for minimally invasive treatment in multiple sclerosis or spinal cord injuries, that use of botulinum toxin is the most effective treatment to reduce NDO.

And for spasticity, there are three products as listed on the slide that are indicated. The Interdisciplinary Working Group for Movement Disorders recommendations in 2017 In multiple sclerosis assert that specialists may consider botulinum treatment for patients with MS. The AAN guideline notes that the three products should be consider for upper-limb spasticity and abobotulinumtoxinA and onabotulinumtoxinA are also established as effective and should be offered for lower-limb spasticity. And then finally, the Canadian practice guidelines for stroke rehabilitation in 2015 asserts that the

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botulinum toxin may be used to treat spasticity and they also do mention other treatment options as well.

So, the final two indications so for strabismus OnabotulinumtoxinA is indicated for this condition. In terms of guidelines, the Pediatric Ophthalmology/Adult Strabismus Preferred Practice parameter along with the American Association for Pediatric Ophthalmology and Strabismus Adult Task Force guidelines in 2020 assert that patients who are not responding to initial treatment with prism which is basically corrective lenses to manage the condition may consider use of onabotulinumtoxinA or surgery for cases that do not resolve. Then the American Optometric Association issued guidelines for adults and children in 2011. They note that the product may be considered as an alternative or as adjunctive treatment to surgery.

And then finally, for Urinary incontinence onabotulinumtoxinA is the only product with indications. The American Urological Association and Society of Urodynamics guidelines in 2019 assert that the product may be offered as a third-line treatment option for patients who are refractory to both first- and second-line treatments. And like OAB, the first-line treatment consists of behavioral therapy, so this would be bladder training, and then second-line treatments include antimuscarinics and beta-3-adrenoceptor agonists.

Okay so switching gears here to the Utilization analysis in terms of the methodology the data source was the Medicaid Data Warehouse. We used timeframe of April 1, 2020 – June 30, 2021. The sample included members enrolled in the NYS Medicaid Program and the fee for service and managed care with either a medical or pharmacy claim for a botulinum toxin during the timeframe. And then in terms of the diagnosis look-back we used a timeframe of 365 days from the index claim for each drug. And then there were several exclusions: So, we did not include NDCs for drugs that have cosmetic purposes. So, for example for treating wrinkles and we excluded the agent prabotulinumtoxinA. Other exclusions include null NDC on the J code, J code NDC mismatch, and duplicate pharmacy claims. And then one of the limitations of our data is while time periods analyzed take into account inherent delays, in terms of the claim, in an encounter submission, data may not be fully complete. Next slide, please. And then in terms of the methodology of the generic brand/manufacturer of the different products that we are using analysis are provided, so you can see how the products are supplied, and then the included NDCs are also listed on the right. And then, I don't think this has been mentioned yet, but in terms of the Medicaid Confidential Data Cell Size Policy, so this requires that no cell containing a value of one to 30 be reported. So, the cell size value must be reported as 30 or less in all public-facing documents. And additionally, no cell can be reported that allows a value of one to 30 to be derived from other reported cells or information. Next slide, please. Okay, so in terms of the overall utilization in pay for service and managed care, the highest utilization was for onabotulinum Botox products. So roughly, there were 12,000 members and approximately 37,000 services, with an average of 3.1 services per member. The next most common was the incobotulinumtoxinA products, trade name Xeomin, with 341 members, 925 services, with an average of 2.7 services per member, and then abobotulinum and rimabotulinum had lower levels of utilization as shown on the slide. Next slide, please. So, this focus is on members with the centers for Medicare and Medicaid services approved diagnosis in

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fee for service plus managed care. As noted on the slide, we only focus on the onabotulinumtoxinA and the incobotulinumtoxinA products. We excluded the other two products, specifically Dysport and Myobloc, as they had low utilization. So, again, in terms of CMS diagnosis, so this included ICD-10 codes that are approved by CMS and that were provided in their billing and coding. So, in terms of the number of members, these are the same as reported on the previous slide for both of the products to roughly 12,000 members for onabotulinumtoxinA and 341 for incobotulinumtoxinA. In terms of a CMS approved chronic migraine diagnosis, so this only applies to the onabotulinum product, as the other products do not have that indication, so there were roughly 6,000 members representing 47 percent who did have the chronic migraine diagnosis. Looking at other CMS approved nonchronic migraine diagnoses, so that is going to be the other approved indications, and the numbers here are not reflected in the previous row, so there are roughly 4,700 members or 40 percent who did have a better CMS approved nonchronic migraine diagnosis. And then for overall CMS approved ICD-10 diagnosis in the previous two rows, there was roughly 10,000 or 87 percent for onabotulinumtoxin, and then for the incobotulinumtoxin, and I apologize, I didn't mention the other CMS non-CM diagnosis, there was 260, representing 76.2 percent. So, overall, we had about 87 and 76 percent of members who received onabotulinumtoxinA and incobotulinumtoxinA, respectively, did have evidence of a CMS-approved ICD-10 diagnosis. Next slide, please. So, this basically kind of summarizes the opposite scenario, so it is summarizing members without a CMS approved diagnosis in fee for service and managed care. Again, the numbers are recorded on top of the slide for each of the two drugs, looking specifically at migraine headache diagnoses that are not accepted by CMS, so there are 613 members or 5.2 percent, and then also looking at other diagnoses not accepted by CMS, and these were not included in the previous row, so there were 350 members or 2.9 percent, and then in terms of no indication at all, and again, these numbers are not reflected in the previous two rows. There were 574 for 4.8 percent for onabotulinumtoxinA, and then for the incobotulinumtoxinA, there were 81 members or 23.8 percent. And so overall, 12.9 percent of members who received onabotulinumtoxinA did not have a CMS -approved ICD-10 diagnosis. Next slide, please. Okay, so the final part of our analysis is the focus on therapy, specifically for the chronic migraine indication. Again, this is for fee for service plus managed care. So, we only reported that there be data for chronic migraine, as the utilization for the other indications was low. So what we looked at is, we looked at members who had at least one claim for a therapy agent prior to starting on a botulinumtoxinA, and so in terms of, so this all for migraine prevention, and for the spectrum that we used, these are both FDA approved or supported, so they included amitriptyline, several beta blockers, topiramate and venlafaxine. So, in terms of the number of members on OnabotulinumtoxinA, this is for our analysis period of April 1, 2020, through June 30, 2021, again we have just the 12,000 members who received OnabotulinumtoxinA, and then looking specifically at new starts, which is the number of members who started the product between July 1, 2020, and June 30, 2021, we had approximately 7,400 members who started the product, and of these members, approximately 2,000 did have at least one plan for a step therapy agent, so that was 28 percent. So, of these



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members that we looked at diagnoses, in terms of CMS approved product migraine diagnosis, there were approximately 2,900 members and of those members, 1,374, 47.6 percent did have evidence for step therapy. When we looked at other CMS approved nonchronic migraine diagnoses, so this excludes the previous row, there were roughly 3,400 members who received the product, and then of these, 453 did have evidence of step therapy, so 13.3 percent. And then finally, overall for CMS approved ICD-10 diagnoses, so this is simply the sum of the two previous rows. There were 6,296 members, and then of these, 1,827 members did a step therapy, accounting for 29 percent. And then finally looking at some migraine headache diagnoses that were not accepted by CMS, there were 402 members who received the products, and of these, 179 or 44.5 percent did have step therapy. For the other diagnoses not accepted by CMS, and this does include these previous drugs, there were 276 members, and then of the 31 or 11.2 percent that did attempt step therapy. And then finally, for no indications, these members could not be included in the previous rows, there were 439 members who started OnabotulinumtoxinA, and then of these, 40 did a step therapy or 9.1 percent. So, a lot of information was presented there. But just to kind of summarize, roughly 48 percent of members who did have the CMS approved chronic migraine diagnoses did attempt step therapy with at least one migraine agent before starting OnabotulinumtoxinA. Next slide, please. So, in conclusion, based on FDA-approved labeling and guideline/consensus statement recommendations, the following indications do have other agents that are recommended as first-line before using a botulinum toxin product: axillary hyperhidrosis, chronic sialorrhea, headache prevention in chronic migraine, overactive bladder, neurogenic detrusor overactivity, strabismus, and urinary incontinence. In terms of the utilization in fee for service plus managed care, the majority was for the onabotulinumtoxinA products, followed by incobotulinumtoxinA. Most members (87 percent) who received onabotulinumtoxinA did have a CMS-approved ICD-10 diagnosis, and then finally, nearly 48 percent of members with a CMS-approved chronic migraine diagnosis attempted step therapy with at least one migraine agent prior to onabotulinumtoxinA. Next slide, please. So there are two recommendations that UB is making to the Department of Health. The first is to recommend a diagnosis requirement for covered indications. So this would exclude coverage for indications which involve cosmetic purposes, so it would exclude treating wrinkles basically. Next slide, please. And then the second recommendation involves implementing step therapy for the following indications: For chronic sialorrhea, where the guideline recommended a trial with glycopyrrolate before using botulinum toxin. However, it did exclude patients with Parkinson's and other neurodegenerative diseases as the botulinum toxin is recommended as first-line. For headache prevention in patients with chronic migraine, this would require a trial with two approved oral preventive agents, and those are listed on the slide, and these are all FDA supported. And then for overactive bladder, guidelines require a trial with an antimuscarinic or beta-3-adrenoceptor agonist. For neurogenic detrusor overactivity, this would require a trial with an antimuscarinic and would exclude patients with multiple sclerosis or spinal cord injury as botulinum toxin are considered to be the most effective treatment to reduce neurogenic detrusor overactivity. And then finally for urinary incontinence, this would require a trial with an

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antimuscarinic or beta-3-adrenoceptor agonist. So that concludes my presentation. I would be happy to take any questions.

Tony Merola: Great. Thank you, Holly.

Holly Coe: Actually, I do want to point out, you may have noticed that for one of the indications for axillary hyperhidrosis, I did not include that in the acceptor requirements. You may remember that topical products are recommended before a botulinum product, and the reason why that is not included here is the products, aluminum chloride is currently not covered by fee-for-service program.

Douglas Fish: Okay, thank you. Questions for Holly on her presentation? No questions? Okay. So, if there are no questions, comments, or discussion, I think we will look for a motion to move to the DOH recommendations. Do I have a motion?

Marla Eglowstein: I move. I move.

Brock Lape: Second.

Douglas Fish: Okay, Marla and Brock, thank you. Tony, you are up.

Tony Merola: Sure, so this is a much shorter slide deck in terms of recommendations from DOH to the DUR Boards, so, Georgie, if you want to go to the second slide here, this mirrors the second slide on the previous review that we did for 4:24:22, so coverage policy with confirm the coverage criteria as we call it, and then the pharmacy will confirm FDA approved use in accordance with FDA packaged labeling or compendious support use, and then we provide a little more clarification and added the phrase for Medicaid covered indication, knowing that some of the products here, as Holly described, are not, have indications for non-Medicaid covered indications, cosmetic use would be a non-covered Medicaid indication, so we did add that clarification there, and then the following recommendations are based upon a review of what Holly had just gone over for us. The available drug information guidelines in the drug utilization that Holly had included in her presentation. So, the recommendations themselves, we actually included them in one page, and that is on the next slide, so Georgie goes to that, and it is basically our step therapy recommendations or trial of a product in the right-hand column, for the indication in the left-hand column. So, that is how we set this out, and we did it in one table rather than having multiple slides over multiple indications. So, I will just read through them, Doug, and then we can open it up for a vote. So, for the indication of chronic sialorrhea, it would be a trial with glycopyrrolate before a botulinum toxin, and it would exclude patients with Parkinson's and other neurodegenerative diseases as that notates. The second one being, the indication being headache prevention in patients with chronic migraine. It would require a trial of two agents, FDA approved or compendia supported for the prevention of migraine. For the overactive bladder indication, it would require a trial with an antimuscarinic agent or beta-3-adrenoceptor agonist. For neurogenic detrusor overactivity, it would require a trial with an antimuscarinic agent, and that would exclude patients with multiple sclerosis or spinal cord

injury. And then the last indication here is urinary incontinence due to detrusor overactivity. It would require a trial with an antimuscarinic agent or beta-3-adrenoceptor agonist. So, those are the recommendations.

Douglas Fish: Thank you, Tony. Comments, questions, or discussions on the DOH recommendations regarding botulinum toxins? Five indications, chronic sialorrhea, chronic headache prevention in patients with chronic migraine, overactive bladder, neurogenic detrusor overactivity, and urinary incontinence due to detrusor overactivity. Any comments? Looking in the chat here too. Okay. I think this is straightforward. So, we will go ahead and move to a vote. Any abstentions? Any opposed? Okay, with that, it passes, and the member tally is 12. We have one fewer member from the attendee list, so we still have forum.

Tony Merola: Okay, after John Powell left, it was 13. We had somebody else exit.

Douglas Fish: That is correct.

Tony Merola: Okay, thank you.

Douglas Fish: Verified by Ms. Lenard. Okay, now we will move to our next presentation on the infliximab therapy, so I am going to turn it over to Xiu Yen, from SUNY Buffalo, so welcome.

Tzu-Yin Kuo: Can everyone hear me okay?

Douglas Fish: Very well.

Tzu-Yin Kuo: Hello?

Douglas Fish: You cut out there for a moment. Let's try it again. We were hearing you, and then it left a second.

Tzu-Yin Kuo: How about now? Is it better?

Douglas Fish: Yes.

Tzu-Yin Kuo: Okay. Good afternoon, everyone. My name is Tzu-Yin. I am a pharmacist fellow at the University of Buffalo. This presentation is for drug revises, a review of infliximab products, including Remicade, Inflectra, Renflexis, and Avsola. Before I get started, I would like to acknowledge my presenters in UB faculty team who have provided help along the way, especially Dr. Barb Rogler and Dr. Brenda Basile. They have helped me a lot to develop the report and the presentation. Next slide, please. The purpose of the presentation is to develop a clinical policy for infliximab products based on currently available literature and peer-reviewed guidelines. Infliximab is a practitioner-administered drug and is currently covered under medical benefits in the fee-for-service program. During this presentation, we will also evaluate the utilization of infliximab products across the New York State Medicaid Program. Remicade is the reference product, and Inflectra, Renflexis, and Avsola are the biosimilars. Next slide, please. Infliximab is a tumor necrosis factor inhibitor and has six FDA-labeled indications.

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Crohn's disease and ulcerative colitis in patient six years of age or above, adult rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and plaque psoriasis. For Crohn's disease or CD, Infliximab is indicated for induction and maintenance of remission in patients with moderate to severe CD who have had an inadequate response to conventional therapy. It is also indicated for reducing the number of draining enterocutaneous and rectovaginal fistulas and maintain fistula closure in adults. For ulcerative colitis or UC, it is indicated for induction and maintenance of remission and mucosal healing, and eliminating corticosteroid use in adults with moderately to severely active UC who have had an inadequate response to conventional therapy. It is also indicated for induction and maintenance of remission in pediatric patients with moderately to severely active UC who have had an inadequate response to conventional therapy. For rheumatoid arthritis or RA, Infliximab can be used in combination with methotrexate or MTX to reduce the signs and symptoms, inhibit the progression of structural damage, and improve the physical function. For ankylosing spondylitis, or AS, it can be used to reduce the signs and symptoms of active AS. For psoriatic arthritis, or PSA, it can be used to reduce the signs and symptoms of active arthritis, inhibit the progression of structural damage, and improve the physical function. For plaque psoriasis, or PS, it can be used in the treatment of chronic, severe plaque psoriasis in patients who are candidates for systemic therapy and when other systemic therapies are medically less appropriate. Next slide, please. Next slide reviews the current coverage data for the TNF inhibitor class. Humira, Cimzia, Enbrel, and Simponi are subject to the preferred drug program, and Humira and Enbrel are the preferred drugs on the PDL. Infliximab products are practitioner administered drugs and are not subject to the PDP. Current clinical criteria associated with TNFi in the immunomodulators systemic category include to confirm diagnosis for FDA- or compendia-supported use and trial of a DMARD prior to treatment with an immunomodulator. Next slide, please. This is a summary of TNFI indications. As you can see, Adalimumab and Etanercept have similar indications of Infliximab. They can be used in pediatric patients with juvenile idiopathic arthritis or JIA, but Infliximab does not have the FDA approved indication. Adalimumab can also be used for patients with hidradenitis suppurativa, or HS, and uveitis. While use of Infliximab for these indications are only compendia supported. Next slide, please. Maintenance dosing frequency is something to be considered as well. Adalimumab is administered every other week for all indications. Dosing for Golimumab is Certolizumab is every four weeks for most indications. For Etanercept, it is once weekly. These agents are all subcutaneous and self-administered injections. On the other hand, Infliximab is an IV infusion for at least two hours every eight weeks for CD, UC, RA, PsA, and plaque psoriasis, and every six weeks for ankylosing spondylitis. Next slide, please. Okay, now let's move onto guideline recommendations. During this presentation, we will cover guideline recommendations for rheumatoid arthritis, Crohn's disease, and ulcerated colitis, as these are the most common indications our members use for. So, here is the 2021 American College of Rheumatology recommendations for RA. For DMARD-naïve patients, DMARD therapy should be started as soon as possible. At first-line therapy for moderate-to-high disease activity RA is MTX methotrexate monitors. For DMARD naïve patients with low disease activity, the preferred agent is Hydroxychloroquine. For patients taking maximally tolerated

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MTX doses but still not at target, add biologic bDMARD or target synthetic tsDMARD instead of using triple conventional synthetic DMARD monitors. bDMARD would include TNF etanercept inhibitors. And the tsDMARD includes JAK inhibitors listed below. For patients who exhibit moderate-to-high disease activity that have taken other csDMARD, except methotrexate, switching to MTX therapy is recommended over going straight to combination therapy with MTX plus either bDMARD or tsDMARD. For patients taking a bDMARD or tsDMARD who are still not at target, switching to a different class is recommended. Next slide, please. Next, we will talk about 2021 American Gastroenterological Association recommendations for adult outpatients with moderate-to-severe luminal and fistulizing CD. For induction of remission of moderate-to-severe CD, AGA suggests using corticosteroids over no treatment. Introduce biologic with or without an immunomodulator early rather than after failure or corticosteroids or five ASA. For patients naïve to biologics, infliximab/adalimumab/ustekinumab is recommended over certolizumab pegol and vedolizumab is suggested over certolizumab pegol. Monotherapy with biologic is recommended thiopurine. Just an FYI, ustekinumab is between 12 and 23 antagonists. For patients that have had an adequate response to TNFi, AGA recommends ustekinumab and suggests using vedolizumab. For patients that relax after initial response to Infliximab, HGA recommends adalimumab or ustekinumab and suggests vedolizumab. If adalimumab was used previously, there was indirect evidence suggesting using infliximab. For induction of fistula remission in patients with CD and active perianal fistula without perianal abscess, AGA recommends using combination therapy with biologic plus antibiotics over using biologic monitors. Use of antibiotic alone as therapy is not suggested. Next slide, please. For induction and maintenance of remission of moderate to severe CD, AGA recommends using TNFi or ustekinumab. Among the PMSI, infliximab or adalimumab is recommended over certolizumab pegol. Monotherapy with vedolizumab or MTX is suggested. This should only be subcutaneous or intramuscular MTX because use of oral MTX, natalizumab, 5-ASA, or sulfasalazine is not suggested. For patients naïve to biologics and immunomodulators, combination therapy was either infliximab or adalimumab plus a thiopurines is suggested over infliximab or adalimumab monotherapy. There is also indirect evidence that suggests using either a combination of either infliximab or adalimumab plus MTX over monotherapy. For induction and maintenance of fistula remission in patients with CD and active perianal fistula, AGA recommends infliximab and suggests adalimumab, ustekinumab or vedolizumab. For maintenance of remission, use of corticosteroid is not recommended. Maintenance of remission in quiescent moderate to severe CD or corticosteroid-induced remission, AGA suggests using thiopurines. Next slide, please. This slide is for the 2020 AGA recommendations for adult outpatients with moderate-to-severe UC. For induction of remission for patients naïve to biologics, Infliximab or vedolizumab is recommended over the standard dose of adalimumab or golimumab. Patients with less severe disease may reasonably choose self-administered subcutaneous adalimumab for their convenience. It was also noted that there was significant evidence to inform a place in therapy for tofacitinib in this patient population. For patients who previously received infliximab (particularly those with primary nonresponse), AGA recommends using ustekinumab or tofacitinib over vedolizumab or adalimumab. Use of

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thiopurine or MTX monotherapy is not suggested. Next slide, please. For induction and maintenance of remission of moderate-to-severe UC, introduce biologic with or without immunomodulator early rather than gradual step up after failure of 5-ASA, except in patients with less severe disease. Use of infliximab, adalimumab, golimumab, vedolizumab, ustekinumab, or tofacitinib is recommended over no treatment. Only use of tofacitinib after failure or intolerance to TNFi. Combination therapy with TNFi or vedolizumab or ustekinumab plus a thiopurine or MTX is suggested over a biologic or thiopurine monotherapy. MTX monotherapy is not suggested. For maintenance of remission, AGA suggests thiopurine monotherapy over no treatment is. There were no recommendations made for biologic or tofacitinib monotherapy vs. thiopurine monotherapy. For patient that have achieved remission with biologics and/or immunomodulators or tofacitinib, continuing 5-ASA is not suggested. Use of MTX monotherapy is not suggested. Next slide, please. That concludes the data recommendation section. Now let's move onto utilization analysis. Our data source is Medicaid Data Warehouse. Members who received infliximab during January 1, 2020, through December 31, 2021, were included. Pharmacy claims and HCPCS codes specific to infliximab were included. Infliximab-specific HCPCS codes with an incorrect NDC were excluded. Next slide, please. The limitation of this analysis, as Holly mentioned earlier, is not being able to report cell value of 30 and below, and cell value of 1 to 30 that can be derived from other report cells or information. There can be delays in claim submissions to NBW, so we may not have a complete data set. Next slide, please. During the two-year period, more than 4,200 members received infliximab. This includes fee for service and managed care members. From 2020 to 2021, the number of members utilizing infliximab increased by 16.7 percent. Next slide, please. During the two-year period, there were more than 44,000 services and pharmacy claims, with a 21.0 percent increase in both claims. Next slide, please. We conducted a diagnosis evaluation to determine if the member had an FDA-approved or compendia-supported indication. Members were included in the analysis if they started infliximab therapy during the timeframe of January 1, 2021, through December 31, 2021. We found that 88 percent of members were using infliximab for FDA-approved indications and nine percent of members were using infliximab for a compendia-supported indication. Next slide, please. This is a summary of the presentation. Infliximab is FDA approved for RA, PsA, plaque psoriasis, AS, CD, and UC. According to FDA-approved labeling, treatment for CD and UC have other agents recommended as first-line prior to using infliximab. And according to guideline recommendations, consider the implementation of step therapy of a csDMARD or an FDA-approved, self-administered TNFi before infliximab. In fee for service and managed care members, most of the utilization was for CD and/or UC. Next slide, please. Now, I would like to present the UB recommendations to DOH for Infliximab clinical policy change. We recommend prescribers to provide a diagnosis that are covered indications. We also recommend considering implementation of step therapy. Use of these modifying antirheumatic drug TNFi, FDA approved for self-administration before starting infliximab. That concludes my presentation. Thank you for your attention. Please let us know if you have any questions.

Douglas Fish: Very good. Thank you, Tzu-Yin, and we are going to give you a Nobel prize for the proper pronunciation of all the monoclonal antibodies. Nice job. Questions, comments, discussion for Tzu-Yinn? It was pretty clear. Any comments? So, we may have been muted for a time, just going to doublecheck. Since we came back, Georgia? Okay. Apologizes if there was a gap. There was a gap. So, comments, questions, or discussion on Tzu-Yin's presentation? Since we were muted, I want to repeat, Tzu-Yin,

Male: Could you speak up a little, sorry?

Douglas Fish: Yeah, Tzu-Yin, we have awarded you a Nobel prize for the proper pronunciation of all the monoclonal antibodies. You may have been muted when I said that the first time, so thank you. Any questions, comments? Okay. Hearing none, then I will ask for a motion to move to the DOH recommendations. So, do I have a motion to discuss?

Female: So moved.

Douglas Fish: Great, we have a motion. And a second?

Male: Second, Doug.

Douglas Fish: Thank you. Tony?

Tony Merola: Okay, so the DOH recommendations to the board are here. Georgia, if you want to do the second slide, it is the standard size that they have been using this afternoon, so the coverage policy will confirm the FDA-approved use in accordance with FDA package labeling and compendia-supported use. And then the following recommendation, we just have one in this case, the following recommendation is based on a review of currently available drug information, guidelines, and the drug utilization review that we just had by Tzu-Yin. So, the recommendation here is step therapy, trial of a disease modifying antirheumatic drug or DMAR or tumor necrosis factor inhibitor, a TNF inhibitor, FDA approved for self-administration prior to initiation of infliximab, so again, it is a trial of a DMAR or a TNF, FDA approved for self-administration, prior to initiation of infliximab.

Douglas Fish: Thank you, Tony. Comments, questions, or discussions on this DOH recommendation? Okay, hearing none, I don't see any comments in the chat. We will move forward with a vote. Anybody abstaining? Any opposed? Okay, this passes with a vote of 12. Thank you. So, next and last topic is, Tzu-Yin, you are up again, I think. So, keep your run going here with these monoclonal antibodies. Georgia will pull up your presentation here.

Tzu-Yin: Can everyone still here me okay?

Douglas Fish: Yes, we can.

Tzu-Yin: Okay. Let me know at one point if you cannot hear me. Tzu-Yin, again. This presentation is for drug utilization review of Entyvio (vedolizumab). Next slide, please. The purpose is to develop a clinical policy for vedolizumab based on currently available literature

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and guidelines. Vedolizumab is an integrin receptor antagonist indicated for the treatment of moderately to severely ulcerative colitis and Crohn's disease (CD) in adults. During this presentation, we will also evaluate the utilization of Vedolizumab across the New York State Medicaid Program. Vedolizumab is a practitioner-administered drug and is currently covered under medical benefit in the fee-for-service program. Next slide, please. Next steps reviewed the current covered data for the TNFi's TNFi class and Vedolizumab. Humira, Cimzia, Enbrel, and Simponi are TNFi subject to the preferred drug program. Humira and Enbrel are preferred drugs on the PDL. Infliximab products and Entyvio are practitioner-administered drugs and not subject to the PDP. Current clinical criteria associated with TNFi in the immunomodulators, and systemic category include a confirmed diagnosis for FDA or compendia-supported use, and trials of DMARD prior to treatment with an immunomodulator. Next slide, please. This is a brief summary on TNFi indications compared to Vedolizumab. So, as you can see, Adalimumab and infliximab have similar indications as Vedolizumab when it comes to CD and UC. Adalimumab and infliximab can be used in pediatric patients, but Vedolizumab can only be used in adults. Next slide, please. Maintenance dosing frequency is important as well. Adalimumab is administered every other week for all indications. Dosing frequency for Golimumab and Certolizumab Pegol is every four weeks for most indications. For Etanercept is once weekly. These are all subcutaneous injections. Dosing frequency for infliximab is every eighth week for most indications. Vedolizumab is an IV infusion for at least 30 minutes. Dosing frequency is every eight weeks for both CD and UC. Next slide, please. Now, we are going to move onto AGA recommendations. This section will be familiar to all we have discussed. So, this slide is for the 2021 American Gastroenterological Association recommendations for adult outpatients who have moderate to severe luminal and fistulizing CD. For induction of remission, AGA suggests using corticosteroids over no treatment. Introduce a biologic with or without an immunomodulator rather than after failure of 5-ASA and/or corticosteroids. For patients naïve to biologics, use of infliximab/adalimumab/ustekinumab is recommended over certolizumab pegol, and use of vedolizumab is suggested over certolizumab pegol. Monotherapy with biologic is recommended over thiopurine. For patients that have had an adequate response to TNFi, AGA recommends using ustekinumab and suggests vedolizumab. For patients that relapse after an initial response to infliximab, AGA recommends using adalimumab or ustekinumab and suggests vedolizumab. If adalimumab was used previously, indirect evidence suggests using infliximab. For induction of fistula remission in patients with CD and active perianal fistula without perianal abscess, combination therapy with a biologic and an antibiotic is recommended over biologic monotherapy. Next slide, please. For induction and maintenance of remission of moderate to severe CD, AGA recommends TNFi or ustekinumab. Monotherapy with vedolizumab or MTX is suggested. And again, this should only be subcutaneous or IM MTX. Use of oral MTX, natalizumab, 5-ASA, or sulfasalazine is not suggested. For patients naïve to biologics and immunomodulators, infliximab or adalimumab combined with thiopurine is suggested over infliximab or adalimumab monotherapy. There is also indirect evidence suggests using infliximab or adalimumab combined with MTX over monotherapy. For induction and maintenance of fistula remission in patients with CD and active perianal fistula, AGA



recommends infliximab and suggests adalimumab, ustekinumab or vedolizumab. For maintenance of remission, use of corticosteroid is not recommended. In quiescent moderate to severe CD or corticosteroid-induced remission, AGA suggests using thiopurines. Next slide, please. Now this slide is for the 2020 AGA recommendations for adult outpatients with moderate-to-severe UC. For induction of remission in patients naïve to biologics, using infliximab or vedolizumab is recommended over the standard dose of adalimumab or golimumab. Patients with less severe disease may choose self-administered subcutaneous adalimumab for their convenience. And again, it was noted that there is limited evidence to inform of therapy of vedolizumab in this patient population. For patient who previously received infliximab (particularly those with primary nonresponse), use of ustekinumab or tofacitinib is recommended over vedolizumab or adalimumab. Use of thiopurine or MTX monotherapy is not suggested. Monotherapy with biologic, such as TNFi or vedolizumab or ustekinumab or tofacitinib is suggested over thiopurine. Next slide, please. For induction and maintenance of remission of moderate to severe UC, introduced biologic with or without immunomodulator early rather than gradual step up after failure of 5-ASA, except in patients with less severe disease. Use of infliximab, adalimumab, golimumab, vedolizumab, ustekinumab, or tofacitinib is recommended over no treatment. Combination therapy was either TNFi, vedolizumab, ustekinumab plus a thiopurine or MTX is suggested over biologic or thiopurine monotherapy. MTX monotherapy is not suggested. For maintenance of remission, AGA suggests using thiopurine monotherapy over no treatment. There were no recommendations made for biologic or tofacitinib monotherapy versus thiopurine monotherapy. For patients that achieved remission with biologics and/or immunomodulators or tofacitinib, continuing using 5-ASA is not suggested. Use of MTX monotherapy is again not suggested. Next slide, please. This slide shows the utilization analysis using data from the Medicaid Data Warehouse. Our inclusion criteria is members who received vedolizumab during January 1, 2020, through December 31, 2021. Both pharmacy claims and HCPCS codes specific to vedolizumab were included. We excluded vedolizumab-specific HCPCS codes with an incorrect NDC. Next slide, please. The limitation of this analysis includes not being able to report cell value of 30 and below and cell value of one to 30 that can be potentially derived from other report cells or information. There can be delays in claim submissions from the Medicaid Data Warehouse, and we may not have a complete data set. Next slide, please. So here are our results. From 2020 to 2021, more than 1,500 members received vedolizumab. This includes fee for service and managed care members. The number of members utilizing vedolizumab increased by 16.4 percent. Next slide, please. From 2020 to 2021, there about 13,000 vedolizumab services and pharmacy claims, and there was a 23 percent increase in those claims. Next slide, please. We also conducted diagnosis evaluation to determine if the member had an FDA-approved or compendia-supported indication. Members were included in this analysis if they started vedolizumab therapy during January 1, 2021, through December 31, 2021. And 457 members were identified. The majority of members were using vedolizumab for an FDA-approved indication, and only less than 30 members did not have a documented FDA-approved indication. Next slide, please. This is a summary of the presentation. Vedolizumab is FDA approved for the treatment of moderate to

severe CD and UC. According to treatment guidelines for CD, a TNFi with either infliximab or adalimumab or ustekinumab is recommended for induction and maintenance of remission, and while use of vedolizumab or MTX is only suggested. According to treatment guidelines for UC, use of infliximab, adalimumab, golimumab, vedolizumab, ustekinumab, or tofacitinib is recommended over no treatment for induction and maintenance of remission. In fee for service and managed care programs, most members were using vedolizumab for an FDA-approved indication. Next slide, please. Now, I would like to present UB recommendations to DOH for Vedolizumab clinical policy change. We recommend prescribers to provide a diagnosis that is a covered indication. We also recommend considering implementation of step therapy. Use of DMARD or a TNFi before starting vedolizumab. That concludes my presentation. Thank you for your attention, and please let me know if you have any questions.

Douglas Fish: Thank you very much, Tzu-Yin. Do we have any questions on the presentation? Did we wear everybody down? It has been a long day. I will answer questions before we go to the DOH recommendations. Okay, do I have a motion to move to the DOH recommendations?

Brock Lape: Motion moved.

Douglas Fish: Perfect, thank you, Brock. A second?

Casey Quinn: Seconded.

Douglas Fish: Thank you, Casey. Okay, Tony, you are up.

Tony Merola: Yup. Okay, Georgia, you can jump to the second slide. We have seen this slide before a couple of times today, so the coverage policy will confirm FDA-approved use in accordance with FDA package labeling or compendia-supported use, and again, this is our DOH recommendation to the board for Vedolizumab, brand name Entyvio. And then we do have, we have one recommendation, so the following recommendation is based on a review of currently available drug information, guidelines, and drug utilization that we just went through, presented by Tzu-Yin. And here is the recommendation. Trial of a disease-modifying anti-rheumatic drug, DMARD, or tumor necrosis factor inhibitor prior to initiation of Vedolizumab, so again, trial of a DMARD or TNF inhibitor prior to initiation of Vedolizumab. That is the one recommendation on this topic.

Douglas Fish: Okay, thank you, Tony. Comments, questions, or discussions on this recommendation?

Donna Chiefari: This is Donna. I just have one question. So, would this make it a double step, in other words, we just talked about Infliximab as being subject to a antigen of self-administered options first. Does that make sense?

Barbara Rogler: Tzu-Yin, I will take that question, thank you. Donna, it doesn't make a double step because what we are doing here is we are allowing, we took out the self-administered here on this guideline, excuse me, this recommendation. It is separate, and the reason that we did that

is to allow for if a provider wants to use Infliximab, okay? So, it is not a double step. Well, you know what? Now that you say that, because you have to have a self-administered before you get to Infliximab. It could potentially be considered a double step, but in this case, not for the others, though. I see what you are saying, Donna, and we recognize that.

Donna Chiefari: Yeah, it would trigger another, you know, another edit, I guess, it would trigger another edit, theoretically, but I don't know how the system sets up.

Barbara Rogler: It will go through because, you are right, for Infliximab, right, Remicade, you would have to first use the self-administered, right? And then now, when you go onto the second edit, if you were to use Entyvio, you would either have a DMARD or TNF inhibitor, but if the provider had jumped the step and gotten approval to go without having self-administered, this would allow this, Infliximab, to go here. Does that make sense?

Donna Chiefari: Yes, I think so.

Barbara Rogler: I recognize what you are saying, and you are right. When I first answered the question, I am sorry, I stumbled, and I had to go back and rethink it through, so I am sorry.

Donna Chiefari: No, no, that is fine. Thank you.

Douglas Fish: Other questions? Okay. Hearing none and nothing in the chat, we will vote. Any abstentions on this recommendation? Trial of a disease-modifying anti-rheumatic drug, or tumor necrosis factor inhibitor prior to initiation of Vedolizumab. Hearing no abstentions, any opposed? Hearing or seeing none, this passes 12 to zero. So, I think that brings us almost to the finish line. That was our final presentation. You are probably disappointed there is not more (laughing). I want to thank you for sticking with us all day, and we got up to a bit of a challenging start. Thanks, Tony, and the team for getting us going and going to plan B with the phones. Thanks to all our board members, especially in the middle of the summer. It is not easy. We know you plan around this, and we deeply appreciate that. Thanks to all our SUNY presenters, Dr. Rogler, Holly Coe, Mina Kwon, and Kim Laurenzo, and anybody I might have missed. Nice job today and all the team who helped put this together. I am going to pass it over to Kim for any final words or comments, and then we will go back to Tony to wrap us up.

Kim Leonard: No, I don't have anything else to add except for expressing my appreciation again, especially because this was such a long day, and now I'll send it over to Tony to close it out.

Tony Merola: Okay, thank you, guys, and I will reiterate essentially what Doug and Kim said, I appreciate everyone's patience this morning, trying to get the meeting off the ground. Once we got it off the ground, I think it went pretty well. In addition to that, again, these recommendations from the DUR Board to the Commissioner, so we will proceed in developing a meeting summary and posting that on the website and then getting the recommendations up to the transmittal process to the Commissioner, and then for anyone that has any questions or comments concerning today's proceedings, they may be sent to this email address:

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[dur@health.ny.gov](mailto:dur@health.ny.gov). And with that, if there are no objections, I think we can officially adjourn, and hopefully, everyone has a wonderful rest of the summer. Thanks very much.