My name is Hiten Patadia and I am a Managed Market Liaison with Otsuka Pharmaceutical Development & Commercialization, Inc. Thank you for this opportunity to provide information on ABILIFY MAINTENA® (aripiprazole) to the Silver Scripts State Board. I believe you all have received and/or reviewed the Full Prescribing Information (PI), so I would like to highlight the following key clinical points:

**DISEASE STATE BACKGROUND**

**Schizophrenia**

Schizophrenia is a heterogeneous disorder with a wide range of potential genetic, environmental, and psychosocial factors that may impact its clinical course. Results from several studies suggest that there is substantial inter-patient variability in responses to different antipsychotic medications. Mental health professionals agree that it is important to match antipsychotic agents to individual patients’ needs. Drug utilization management policies that hinder access to medications and continuity of care may interfere with treatment. One study by West et al. examined medication access among psychiatric patients in 10 state Medicaid programs (including CA, FL, GA, MA, MI, NY, OH, PA, TN, TX) to evaluate adverse events associated with medication access issues. Results showed that patients with medication access issues had 3.6x greater likelihood of adverse events, including emergency room visits, hospitalizations, homelessness, suicidality, or incarceration. Based on these findings, it was concluded that access to a full range of medications facilitates optimal disease management for psychiatric patients.

It can be a challenge for physicians to find the most effective treatment for their patients with schizophrenia as well as to ensure that the patient remains adherent. The heterogeneity of both the disorder and treatment response to antipsychotics makes it important to preserve access to treatment. Evidence supports that abrupt discontinuation of oral antipsychotics may precipitate a relapse. Long-acting injectable (LAI) antipsychotics can be an important alternative to oral medications in some patients with schizophrenia, especially those with a history of non-adherence or those who prefer this mode of administration.

**Bipolar Disorder**

Bipolar I (BP-I) disorder is a serious, lifelong, episodic illness characterized by the occurrence of one or more manic episodes. Episodes of mania are recurrent and commonly associated with negative outcomes, including a decline in cognitive function and an increase in hospitalizations; BP-I disorder is associated with significant medical and psychiatric comorbidity, premature death, functional disability, and reduced quality of life. BP-I disorder has also been associated with an increased risk of suicide attempts and completion.

Long-term pharmacologic treatment is necessary to prevent recurrence of symptoms and relapse. The chronic nature of BP-I disorder and the negative consequences of unremitting or recurrent symptoms emphasize the need for effective long-term treatment.

Otsuka Pharmaceutical Development & Commercialization, Inc. supports an open access policy to allow for individualized and appropriate treatment of patients with serious mental illness.

**INDICATIONS AND USAGE**

ABILIFY MAINTENA® (aripiprazole) for extended-release injectable suspension is an atypical antipsychotic indicated for the treatment of schizophrenia and for maintenance monotherapy treatment of BP-I disorder. On July 29th, 2017, ABILIFY MAINTENA® was approved by the U.S. Food and Drug Administration as the first once-monthly long-acting injectable for the maintenance monotherapy treatment of BP-I disorder in adults.

ABILIFY MAINTENA® is for deep intramuscular (IM) deltoid or gluteal injection to be administered by a healthcare professional (HCP) only.

**EFFICACY AND SAFETY**

**Schizophrenia**

**Summary:** The efficacy of ABILIFY MAINTENA® for the treatment of schizophrenia was established in one short-term (12-week) trial in acutely relapsed adults and one longer-term (52 weeks) maintenance trial in adults.

In the 12-week, randomized, double-blind, placebo-controlled trial in acutely relapsed adults, the primary endpoint was the change from baseline in Positive and Negative Syndrome Scale (PANSS) total score to Week 10. The least squares mean change in PANSS total score from baseline for ABILIFY MAINTENA® was -26.8 versus placebo -11.7 at the end of Week 10. The most commonly observed adverse reactions (incidence of ≥5% and aripiprazole incidence at least twice that for placebo) were increased weight (16.8% vs 7.0%), akathisia (11.4% vs 3.5%), injection site pain (5.4% vs 0.6%) and sedation (5.4% vs 1.2%).

The efficacy of ABILIFY MAINTENA® in maintaining symptomatic control in schizophrenia was established in a double-blind, placebo-controlled, randomized-withdrawal trial in adult patients. The final analysis demonstrated a statistically significantly longer time to relapse, which was the primary efficacy endpoint, in patients randomized to the ABILIFY MAINTENA® group than compared to placebo-treated patients (p<0.0001). The key secondary endpoint, percentage of subjects meeting the exacerbation of psychotic symptoms/relapse criteria, was also statistically significantly lower in patients randomized to the ABILIFY MAINTENA® group (10%) than in the placebo group (40%). The most common treatment emergent adverse events (TEAEs; occurring in ≥5% of the subjects in the ABILIFY MAINTENA arm and greater than placebo) were insomnia, tremor, and headache.
Bipolar I Disorder\textsuperscript{11,15}

Summary: The efficacy of ABILIFY MAINTENA for the maintenance treatment of BP-I disorder was established in a 52-week, double-blind, placebo-controlled, withdrawal trial in adult patients with BP-I disorder who were experiencing a manic episode at trial entry (n=266 randomized), met DSM-IV-TR criteria for BP-I disorder, and had a history of at least one previous manic or mixed episode with manic symptoms of sufficient severity to require one of the following interventions: hospitalization and/or treatment with a mood stabilizer, and/or treatment with an antipsychotic agent.

The primary efficacy endpoint was time from randomization to recurrence of any mood episode. Analysis demonstrated a statistically significantly longer time to recurrence of any mood episode in subjects randomized to the ABILIFY MAINTENA group than compared to placebo-treated patients (hazard ratio: 0.45; p<0.0001). The most common TEAEs (occurring in \textgeq 5\% of the subjects in the ABILIFY MAINTENA arm and greater than placebo) were weight increase, akathisia, insomnia, and anxiety.

SAFETY\textsuperscript{11}

In fair balance, I call your attention to the BOXED WARNING for ABILIFY MAINTENA: Increased Mortality in Elderly Patients with Dementia-Related Psychosis. For the complete BOXED WARNING and additional information, please refer to the Full PI for ABILIFY MAINTENA.

PHARMACOKINETICS\textsuperscript{11,16}

ABILIFY MAINTENA activity is presumably primarily due to the parent drug, aripiprazole, and to a lesser extent, to its major metabolite, dehydro-aripiprazole, which has been shown to have affinities for D\textsubscript{2} receptors similar to the parent drug and represents about 29\% of the parent drug exposure in plasma.

Aripiprazole absorption into the systemic circulation is slow and prolonged following IM injection due to low solubility of aripiprazole particles. Following a single dose administration of ABILIFY MAINTENA in the deltoid and gluteal muscle, the extent of absorption (AUC\textsubscript{t}, AUC\textsubscript{∞}) of aripiprazole was similar for both injection sites, but the rate of absorption (C\textsubscript{max}) was 31\% higher following administration to the deltoid compared to the gluteal site.

ABILIFY MAINTENA is formulated to contain aripiprazole and no biotransformation is needed to derive the active drug form. Based on unpublished pharmacokinetic modeling data of ABILIFY MAINTENA and oral aripiprazole tablets, the estimated oral aripiprazole dose equivalence, calculated based on median area under the curve, are approximately 16 mg for the ABILIFY MAINTENA 300 mg dose and 21 mg for the ABILIFY MAINTENA 400 mg dose.

SUMMARY

CONTINUED COVERAGE

In closing, Otsuka Pharmaceutical Development & Commercialization, Inc. respectfully requests that ABILIFY MAINTENA continue to remain available to patients in Nevada with the same access that they have received to date. Upon request, I am happy to provide the committee with any specific medical information you may need.

Please refer to the attached ABILIFY MAINTENA Package Insert for the FULL PRESCRIBING INFORMATION.

REFERENCES:

2. Lane H et al. Pharmacogenomics 2005; 6(2):139-149.
11. ABILIFY MAINTENA® (aripiprazole) FULL PRESCRIBING INFORMATION.
16. Data on file. ABIMAI-007