Proteus Digital Health

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U.S. FDA Accepts First Digital Medicine New Drug Application for Otsuka and Proteus Digital Health

The first Digital Medicine, a drug/device product, combines Otsuka's ABILIFY® (aripiprazole) for serious mental illness, embedded with the Proteus® ingestible sensor in a single tablet to digitally record ingestion and, with patient consent, share information with their healthcare professionals and caregivers

Otsuka and Proteus are pursuing a regulatory filing for a drug-device combination across multiple divisions of the FDA to support the unique system

First opportunity to demonstrate the potential of Digital Medicines to provide an objective measure of medication adherence and physiologic response

TOKYO, JAPAN and REDWOOD SHORES, CALIF. – September 10, 2015 – Otsuka Pharmaceutical Co., Ltd. (Otsuka) and Proteus Digital Health (Proteus) today announced that the United States Food and Drug Administration (FDA) has determined that the New Drug Application (NDA) for the combination product of ABILIFY® (aripiprazole) embedded with a Proteus® ingestible sensor in a single tablet is sufficiently complete to allow for a substantive review and is considered filed as of September 8, 2015.

This is the first time an FDA-approved medication (ABILIFY) has been combined and submitted for approval with a sensor within the medication tablet (the Proteus ingestible sensor) to measure actual medication-taking patterns and physiologic response. This objective information is communicated to the patient – and with the consent of the patient – to the patient's physician and/or caregiver. Digital Medicines may enable improved patient medication adherence and better informed physician decision-making to tailor treatment to the patient's needs.

An estimated average of 50% of patients with chronic diseases in developed countries do not take medicines as prescribed, possibly limiting the effectiveness of those medicines. In the U.S., this may result

in an estimated $100-300 billion in avoidable healthcare costs due to direct costs such as unnecessary escalation of treatment as well as indirect costs.[1],[2] For example, patients suffering from chronic mental disorders such as schizophrenia are often required to take medication for long periods, and it is not unusual for these patients to discontinue taking their medication, or not take their medication as prescribed, which can lead to disease relapse and recurrence.[3],[4]

The ABILIFY tablet contains an ingestible sensor that communicates with a wearable sensor patch and a medical software application for measuring adherence in the treatment of adults with schizophrenia, acute treatment of manic and mixed episodes associated with bipolar I disorder, and as adjunctive therapy for the treatment of major depressive disorder in adults.

“Today, patients suffering from severe mental illnesses struggle with adhering to or communicating with their healthcare teams about their medication regimen, which can greatly impact outcomes and disease progression,” said William H. Carson, M.D., president and CEO of Otsuka Pharmaceutical Development & Commercialization, Inc. “We believe this new Digital Medicine could revolutionize the way adherence is measured and fulfill a serious unmet medical need in this population. We look forward to continuing working with the FDA throughout the NDA review.”

If approved by the FDA, healthcare professionals will have the ability to prescribe ABILIFY tablets with the Proteus ingestible sensor embedded in the tablet. This drug-device product can provide the patient with a treatment option to help manage symptoms while allowing the caregiver and healthcare professional to measure medication adherence and other patient metrics. This unique system is filed as an NDA, where the FDA Center for Devices and Radiological Health (CDRH)-cleared ingestible sensor from Proteus will be embedded at the point of manufacture with the FDA Center for Drug Evaluation and Research (CDER) -approved ABILIFY as a combination drug-device, communicating with the Proteus patch and associated medical software.

“Digital Medicines have the potential to move healthcare beyond the proven efficacy of a medicine to understand the real world effectiveness of a therapy for each individual,” said Andrew Thompson, president and CEO of Proteus Digital Health. “This means that medicines could be tailored to each of us to reflect our unique medication-taking patterns, lifestyle and daily health choices.”

When ABILIFY with the embedded ingestible sensor is taken, the ingestible sensor sends a signal to the wearable Proteus patch after it reaches the stomach. The patch records and time-stamps the information from the ingestible sensor in addition to collecting other patient metrics, including rest, body angle and activity patterns. This information is recorded and relayed to patients on a mobile phone or other Bluetooth-enabled device, and only with their consent, to their physician and/or their caregivers. Patients view the information using a secure and local software application on their mobile phone or device. Physicians and caregivers view the data using secure web portals.

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[1]Sabaté E, editor. *Adherence to long-term therapies: evidence for action.* Geneva, Switzerland: World Health Organization; 2003.

[2]Iuga AO, McGuire MJ. Adherence and health care costs. Risk Management and Healthcare Policy. 2014;7:35-44.

[3] Lehman, AF, Lieberman JA, Dixon LB, McGlashan TH, Miller AL, Perkins DO, et al. Practice guideline for the treatment of patients with schizophrenia, second edition. Am J Psychiatry. 2004 Feb;161(2 Suppl): 1-56.

[4] Masand, PS1, Roca M, Turner MS, Kane JM. Prim care companion. J Clin Psychiatry. 2009;11(4):147-54.

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INDICATIONS and IMPORTANT SAFETY INFORMATION for ABILIFY® (aripiprazole)

INDICATIONS

ABILIFY is indicated for:

- Use as an adjunctive therapy to antidepressants in adults with Major Depressive Disorder who have had an inadequate response to antidepressant therapy
- Acute treatment of manic or mixed episodes associated with Bipolar I Disorder as monotherapy and as an adjunct to lithium or valproate in adult
- Treatment of Schizophrenia in adults

IMPORTANT SAFETY INFORMATION

Increased Mortality in Elderly Patients with Dementia-Related Psychosis

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk (1.6 to 1.7 times) of death compared to placebo (4.5% vs 2.6%, respectively). Although the causes of death were varied, most of the deaths appeared to be cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. ABILIFY is not approved for the treatment of patients with dementia-related psychosis.

Suicidal Thoughts and Behaviors

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of Major Depressive Disorder (MDD) and other psychiatric disorders. Anyone considering the use of adjunctive ABILIFY or another antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increased risk of suicidality in adults beyond age 24. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. ABILIFY is not approved for use in pediatric patients with depression.

See Full Prescribing Information for complete Boxed WARNING

Contraindication – Known hypersensitivity reaction to ABILIFY. Reactions have ranged from pruritus/urticaria to anaphylaxis.

Cerebrovascular Adverse Events, Including Stroke – Increased incidence of cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, have been reported in clinical trials of elderly patients with dementia-related psychosis treated with ABILIFY

Neuroleptic Malignant Syndrome (NMS) – As with all antipsychotic medications, a rare and potentially fatal condition known as NMS has been reported with ABILIFY. NMS can cause hyperpyrexia, muscle rigidity, diaphoresis, tachycardia, irregular pulse or blood pressure, cardiac dysrhythmia, and altered mental status. Additional signs may include elevated creatinine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. Management should include immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy, intensive symptomatic treatment and medical monitoring, and treatment of any concomitant serious medical problems

Tardive Dyskinesia (TD) – The risk of developing TD and the potential for it to become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic increase. The syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. Prescribing should be consistent with the need to minimize TD. The syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn

Metabolic Changes – Atypical antipsychotic drugs have been associated with metabolic changes that include:

Hyperglycemia/Diabetes Mellitus– Hyperglycemia, in some cases extreme and associated with ketoacidosis, coma, or death, has been reported in patients treated with atypical antipsychotics including ABILIFY. Patients with diabetes should be regularly monitored for worsening of glucose control; those with risk factors for diabetes should undergo baseline and periodic fasting blood glucose testing. Any patient treated with atypical antipsychotics should be monitored for symptoms of

hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia should also undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of anti-diabetic treatment despite discontinuation of the suspect drug

Dyslipidemia– Undesirable alterations in lipids have been observed in patients treated with atypical antipsychotics. There were no significant differences between Abilify- and placebo-treated patients in the proportion with changes from normal to clinically significant levels for fasting/nonfasting total cholesterol, fasting triglycerides, fasting LDLs, and fasting/nonfasting HDLs

Weight Gain– Weight gain has been observed with atypical antipsychotic use. Clinical monitoring of weight is recommended. When treating pediatric patients, weight gain should be monitored and assessed against that expected for normal growth

Orthostatic Hypotension – ABILIFY may be associated with orthostatic hypotension and should be used with caution in patients with known cardiovascular disease, cerebrovascular disease, or conditions which would predispose them to hypotension.

Leukopenia, Neutropenia, and Agranulocytosis – Leukopenia, neutropenia, and agranulocytosis have been reported with antipsychotics, including ABILIFY. Patients with history of a clinically significant low white blood cell (WBC) count or drug-induced leukopenia/neutropenia should have their complete blood count (CBC) monitored frequently during the first few months of therapy and discontinuation of ABILIFY should be considered at the first sign of a clinically significant decline in WBC count in the absence of other causative factors.

Seizures/Convulsions – As with other antipsychotic drugs, ABILIFY should be used with caution in patients with a history of seizures or with conditions that lower the seizure threshold (e.g., Alzheimer's dementia).

Potential for Cognitive and Motor Impairment – Like other antipsychotics, ABILIFY may have the potential to impair judgment, thinking, or motor skills. Patients should not drive or operate hazardous machinery until they are certain ABILIFY does not affect them adversely.

Body Temperature Regulation – Disruption of the body's ability to reduce core body temperature has been attributed to antipsychotics. Appropriate care is advised for patients who may exercise strenuously, be exposed to extreme heat, receive concomitant medication with anticholinergic activity, or be subject to dehydration.

Suicide – The possibility of a suicide attempt is inherent in psychotic illnesses, Bipolar Disorder, and Major Depressive Disorder, and close supervision of high-risk patients should accompany drug therapy. Prescriptions should be written for the smallest quantity consistent with good patient management in order to reduce the risk of overdose.

Dysphagia – Esophageal dysmotility and aspiration have been associated with antipsychotic drug use, including ABILIFY; use caution in patients at risk for aspiration pneumonia. Aspiration pneumonia is a common cause of morbidity and mortality in elderly patients, in particular those with advanced Alzheimer's dementia.

Physicians should advise patients to avoid alcohol while taking ABILIFY.

Strong CYP3A4 (e.g., ketoconazole) or CYP2D6 (e.g., fluoxetine) inhibitors will increase ABILIFY drug concentrations; reduce ABILIFY dose by one-half when used concomitantly, except when used as adjunctive treatment with antidepressants in adults with Major Depressive Disorder. If a strong CYP3A4 inhibitor and strong CYP2D6 inhibitor are co-administered or a known CYP2D6 poor metabolizer is receiving a concomitant strong CYP3A4 inhibitor, the ABILIFY dose should be reduced to one-quarter (25%) of the usual dose.

CYP3A4 inducers (e.g., carbamazepine) will decrease ABILIFY drug concentrations; double ABILIFY dose when used concomitantly.

Commonly observed adverse reactions: (≥5% incidence and at least twice the rate of placebo for ABILIFY vs placebo, respectively):

Adult patients with Major Depressive Disorder (adjunctive treatment to antidepressant therapy): akathisia (25% vs 4%), restlessness (12% vs 2%), insomnia (8% vs 2%), constipation (5% vs 2%), fatigue (8% vs 4%), and blurred vision (6% vs 1%)

Adult patients (monotherapy) with Bipolar Mania: akathisia (13% vs 4%), sedation (8% vs 3%), tremor (6% vs 3%), restlessness (6% vs 3%), and extrapyramidal disorder (5% vs 2%)

Adult patients with Schizophrenia: akathisia (8% vs 4%)

Dystonia is a class effect of antipsychotic drugs. Symptoms of dystonia may occur in susceptible individuals during the first days of treatment and at low doses.

Pregnancy: Non-Teratogenic Effects – Neonates exposed to antipsychotic drugs during the third trimester of pregnancy are at risk for extrapyramidal and/or withdrawal symptoms following delivery. These complications have varied in severity; from being self-limited to requiring intensive care and prolonged hospitalization. ABILIFY should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers – ABILIFY is excreted in human breast milk. A decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Please see accompanying FULL PRESCRIBING INFORMATION, including **Boxed WARNING**, for ABILIFY.

About ABILIFY® (aripiprazole)

Discovered by Otsuka Pharmaceutical Co., Ltd., ABILIFY was the first available dopamine partial agonist and is indicated for the acute treatment of manic or mixed episodes associated with bipolar I disorder in adults, the maintenance treatment of bipolar I disorder, treatment of schizophrenia in adults, and as an adjunctive treatment to an antidepressant in adults with major depressive disorder who have an inadequate response to antidepressant therapy. ABILIFY Tablets are available in 2 mg, 5 mg, 10 mg, 15 mg, 20 mg and 30 mg strengths. Otsuka welcomes you to visit its U.S. website for more information about ABILIFY, and its global website for more information about the company.

About the Proteus® Ingestible Sensor and Wearable Patch

The Proteus ingestible sensor and wearable patch have been cleared by the Food and Drug Administration (FDA) for use in the United States, and CE marked per the Medical Device Directive for use in the European Union. More information is available at www.proteus.com.

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