RISPERDAL(R) CONSTA(R) (Risperidone) Long-Acting Treatment Delayed the Time to Relapse in Patients with Bipolar I Disorder

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SAN FRANCISCO, May 19, 2009 – New data demonstrate that maintenance therapy with RISPERDAL® CONSTA® (risperidone) Long-Acting Treatment (RLAT) significantly delayed the time to relapse compared to placebo in patients with bipolar I disorder. Results of the study were presented this week at a major medical meeting.

Bipolar disorder is a brain disorder that causes unusual shifts in a person's mood, energy and ability to function. It is often characterized by debilitating mood swings from extreme highs (mania) to extreme lows (depression). Type I bipolar disorder is characterized based on the occurrence of at least one manic episode, with or without the occurrence of a major depressive episode, and affects approximately one percent of the American adult population in any given year.

A randomized, double-blind, placebo-controlled, long-term study was conducted to evaluate the effect of RISPERDAL CONSTA as maintenance therapy in patients who met DSM-IV criteria for bipolar I disorder who were stable on medications or experiencing an acute manic or mixed episode. In the first phase of the study, 303 patients were stabilized on open-label RISPERDAL CONSTA for 26 weeks. In the double-blind phase, patients were randomized to either maintenance therapy with RISPERDAL CONSTA (N=154) or placebo (N=149). The median duration of treatment was nine months for patients in the RISPERDAL CONSTA group and five months for patients in the placebo group. The primary endpoint was time to relapse of any mood episode (depression, mania, or mixed).

Time to relapse was significantly longer in patients receiving RISPERDAL CONSTA monotherapy as compared to placebo (p 10% in adjunctive therapy)

“This is the first randomized controlled study to demonstrate the efficacy of RLAT as a maintenance therapy in patients with bipolar disorder,” said Joseph Palumbo, M.D., Franchise Medical Leader, Psychiatry, Central Nervous System and Pain Therapeutic Area, Johnson & Johnson Pharmaceutical Research & Development, L.L.C. (J&JPRD). “These findings are important because the clinical course of bipolar disorder is often unpredictable and relapses can be very debilitating.”

The study was presented and sponsored by Janssen, a Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc and J&JPRD.

About RISPERDAL CONSTA Long Acting Treatment

RISPERDAL CONSTA (risperidone) Long-Acting Treatment (RLAT) is a long-acting injectable atypical antipsychotic therapy used for the treatment of schizophrenia and the maintenance treatment of bipolar I disorder. It was developed utilizing Alkermes’ proprietary Medisorb® drug-delivery technology. Using this technology, risperidone is encapsulated in microspheres made of a biodegradable polymer, which are suspended in a water-based solution and administered to patients by intramuscular injection once every two weeks. RISPERDAL CONSTA is manufactured by Alkermes, Inc. and marketed by Janssen, Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc. in the U.S. and Janssen-Cilag outside of the U.S.

IMPORTANT SAFETY INFORMATION FOR CONSUMERS ABOUT RISPERDAL CONSTA

Elderly Patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death compared to placebo. RISPERDAL CONSTA (risperidone) is not approved for the treatment of patients with dementia-related psychosis.

Neuroleptic Malignant Syndrome (NMS) is a rare and potentially fatal side effect reported with RISPERDAL CONSTA and similar medicines. Call your doctor immediately if the person being treated develops symptoms such as high fever; stiff muscles; shaking; confusion; sweating; changes in pulse, heart rate, or blood pressure; or muscle pain and weakness. Treatment should be stopped if the person being treated has NMS.

Tardive Dyskinesia (TD) is a serious, sometimes permanent side effect reported with RISPERDAL CONSTA and similar medications. TD includes uncontrollable movements of the face, tongue, and other parts of the body. The risk of developing TD and the chance that it will become permanent is thought to increase with the length of therapy and the overall dose taken by the patient. This condition can develop after a brief period of therapy at low doses, although this is much less common. There is no known treatment for TD, but it may go away partially or completely if therapy is stopped.

High blood sugar and diabetes have been reported with RISPERDAL CONSTA and similar medications. If the person being treated has diabetes or risk factors such as being overweight or a family history of diabetes, blood sugar testing should be performed at the beginning and throughout treatment with RISPERDAL CONSTA. Complications of diabetes can be serious and even life threatening. If signs of high blood sugar or diabetes develop, such as being thirsty all the time, going to the bathroom a lot, or feeling weak or hungry, contact your doctor.

RISPERDAL CONSTA and similar medications can raise the blood levels of a hormone known as prolactin, causing a condition known as hyperprolactinemia. Blood levels of prolactin remain elevated with continued use. Some side effects seen with these medications include the absence of a menstrual period; breasts producing milk; the development of breasts by males; and the inability to achieve an erection.

Some people taking RISPERDAL CONSTA may feel faint or lightheaded when they stand up or sit up too quickly. By standing up or sitting up slowly and following your healthcare professional’s dosing instructions, this side effect can be reduced or it may go away over time.

Problems with the blood have been reported with RISPERDAL CONSTA and similar medications. Depending upon condition your doctor may choose to monitor your blood as you start therapy with RISPERDAL CONSTA.

RISPERDAL CONSTA may affect your alertness or driving ability; therefore, do not drive or operate machinery before talking to your healthcare professional.

RISPERDAL CONSTA should be used cautiously in people with a seizure disorder, who have had seizures in the past, or who have conditions that increase their risk for seizures.

Painful, long lasting erections have been reported with the use of RISPERDAL CONSTA. Call your doctor immediately if you think you are having this problem.

Extrapyramidal Symptoms (EPS) are usually persistent movement disorders or muscle disturbances, such as restlessness, tremors, and muscle stiffness. If you observe any of these symptoms, talk to your healthcare professional.

Inform your healthcare professional if you become pregnant or intend to become pregnant during therapy with RISPERDAL CONSTA. Caution should be exercised when administering RISPERDAL CONSTA to a nursing woman.

RISPERDAL CONSTA may make you more sensitive to heat. You may have trouble cooling off, or be more likely to become dehydrated, so take care when exercising or when doing things that make you warm.

Some medications interact with RISPERDAL CONSTA. Please inform your healthcare professional of any medications or supplements that you are taking. Avoid alcohol while on RISPERDAL CONSTA.

In a study of people taking RISPERDAL CONSTA, the most common side effects in the treatment of schizophrenia were headache, tremors, dizziness, restlessness, tiredness, constipation, indigestion, sleepiness, weight gain, pain in the limbs, and dry mouth.

In a study of people taking RISPERDAL CONSTA, the most common side effects in the treatment of bipolar I disorder were weight gain (when used alone) and tremors (when used with other medications).

If you have any questions about RISPERDAL CONSTA or your therapy, talk with your doctor.

IMPORTANT SAFETY INFORMATION FOR PROFESSIONALS ABOUT RISPERDAL CONSTA

WARNING: Increased Mortality in Elderly Patients with Dementia-Related Psychosis Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of 17 placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear. RISPERDAL CONSTA (risperidone) is not approved for the treatment of patients with dementia-related psychosis.

Cerebrovascular Adverse Events (CAEs): CAEs, including fatalities, have been reported in elderly patients with dementia-related psychosis taking oral risperidone in clinical trials. The incidence of CAEs with risperidone was significantly higher than with placebo. RISPERDAL CONSTA is not approved for the treatment of patients with dementia-related psychosis.

Neuroleptic Malignant Syndrome (NMS): NMS, a potentially fatal symptom complex, has been reported with the use of antipsychotic medications, including RISPERDAL CONSTA. Clinical manifestations include muscle rigidity, fever, altered mental status and evidence of autonomic instability (see full Prescribing Information). 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): TD is a syndrome of potentially irreversible, involuntary, dyskinetic movements that may develop in patients treated with antipsychotic medications. The risk of developing TD and the likelihood that dyskinetic movements will become irreversible are believed to increase with duration of treatment and total cumulative dose. Elderly patients appeared to be at increased risk for TD. Prescribing should be consistent with the need to minimize the risk of TD. The syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn.

Hyperglycemia and Diabetes: Hyperglycemia, some cases extreme and associated with ketoacidosis, hyperosmolar coma or death has been reported in patients treated with atypical antipsychotics (APS), including RISPERDAL CONSTA. Patients starting treatment with APS who have or are at risk for diabetes should undergo fasting blood glucose testing at the beginning of and during treatment. Patients who develop symptoms of hyperglycemia should also undergo fasting blood glucose testing.

Hyperprolactinemia: As with other drugs that antagonize dopamine D2 receptors, RISPERDAL CONSTA elevates prolactin levels and the elevation persists during chronic administration. Risperidone is associated with higher levels of prolactin elevation than other antipsychotic agents.

Orthostatic Hypotension: RISPERDAL CONSTA may induce orthostatic hypotension associated with dizziness, tachycardia, and in some patients, syncope, especially during the initial dose-titration period. Monitoring should be considered in patients for whom this may be of concern. RISPERDAL CONSTA should be used with caution in patients with known cardiovascular disease, and conditions that would predispose patients to hypotension.

Leukopenia, Neutropenia and Agranulocytosis have been reported with antipsychotics, including risperidone. Patients with a pre-existing low white blood cell count (WBC) or a history of leukopenia/neutropenia should have frequent complete blood cell counts during the first few months of therapy. At the first sign of a decline in WBC and in the absence of other causative factors, discontinuation of Risperdal Consta should be considered.

Potential for Cognitive and Motor Impairment: RISPERDAL CONSTA has the potential to impair judgment, thinking, or motor skills.Patients should be cautioned about operating hazardous machinery, including motor vehicles, until they are reasonably certain that RISPERDAL CONSTA does not affect them adversely.

Seizures: RISPERDAL CONSTA should be used cautiously in patients with a history of seizures or with conditions that potentially lower seizure threshold.

Dysphagia: Esophageal dysmotility and aspiration can occur. Use cautiously in patients at risk for aspiration pneumonia.

Priapism has been reported. Severe priapism may require surgical intervention.

Thrombotic Thrombocytopenic Purpura (TTP) has been reported.

Administration: Care should be taken to avoid inadvertent injection into a blood vessel.

Suicide: The possibility of suicide attempt is inherent in psychotic illnesses. Close supervision of high-risk patients should accompany drug therapy.

Increased sensitivity in patients with Parkinson's disease or those with dementia with Lewy bodies has been reported. Manifestations and features are consistent with NMS.

Use RISPERDAL CONSTA with caution in patients with conditions and medical conditions that could affect metabolism or hemodynamic responses (e.g. Recent Myocardial infarction or unstable cardiac disease).

Extrapyramidal Symptoms (EPS): The overall incidence of EPS-related adverse events in patients treated with 25 mg and 50 mg of RISPERDAL CONSTA and placebo, respectively, were akathisia* (4%, 11%, 6%), Parkinsonism† (8%, 15%, 9%) and tremor (0%, 3%, 0%).

* Akathisia and restlessness
† Extrapyramidal disorder, musculoskeletal stiffness, muscle rigidity, and bradykinesia

Weight Gain: In a 12-week trial, the percentage of patients experiencing weight gain (>7% of baseline body weight) was 6% placebo versus 9% RISPERDAL CONSTA.

Maintenance Treatment: Patients should be periodically reassessed to determine the need for continued treatment.

Commonly Observed Adverse Reactions for RISPERDAL CONSTA: The most common adverse reactions in clinical trials in patients with schizophrenia (≥5%) were headache, Parkinsonism, dizziness, akathisia, fatigue, constipation, dyspepsia, sedation, weight increase, pain in extremities, and dry mouth.

The most common adverse reactions in clinical trials in patients with bipolar disorder trials were weight increase (5% in monotherapy trial) and tremor and parkinsonism (> 10% in adjunctive therapy trial).

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