



U.S. FDA Approves Supplemental New Drug Applications for Once-Monthly Long-Acting Therapy INVEGA® SUSTENNA® (paliperidone palmitate) for the Treatment of Schizoaffective Disorder

November 13, 2014

TITUSVILLE, N.J., Nov. 13, 2014 /PRNewswire/ -- Janssen Pharmaceuticals, Inc. today announced that the U.S. Food and Drug Administration (FDA) approved the supplemental New Drug Applications (sNDAs) for the once-monthly atypical long-acting antipsychotic INVEGA® SUSTENNA® (paliperidone palmitate) to treat schizoaffective disorder as either monotherapy or adjunctive therapy. The symptoms of schizoaffective disorder are complex and, without treatment, disabling. The FDA approved these sNDAs under priority review, which is a designation for drugs that, if approved, would offer significant improvement in the treatment of serious conditions.

INVEGA® SUSTENNA® is the first and only FDA-approved once-monthly medication to treat schizoaffective disorder as monotherapy.

"Clinicians often find themselves taking a complicated approach using multiple medications to address schizoaffective disorder symptoms because widely accepted guidelines for the treatment of the condition are not available," said David P. Walling, PhD, study lead investigator and Chief Executive and Clinical Officer, Collaborative NeuroScience Network, Inc., Los Angeles. "The approval of an effective once-monthly medication that can be used as monotherapy or adjunctive therapy to manage the symptoms associated with schizoaffective disorder has the potential to change that approach."

The approval is based on data from a 15-month period of a long-term maintenance study measuring ability to delay relapse in schizoaffective disorder. The study found that treatment with INVEGA® SUSTENNA® resulted in a statistically significant delay in relapse due to mood (depression and mania) and psychotic symptoms of schizoaffective disorder compared to placebo. Results of the study were presented in May at the 167th Annual Meeting of the American Psychiatric Association.

"Schizoaffective disorder is a difficult-to-treat disease. Approval of INVEGA® SUSTENNA® to manage the mood as well as the psychosis that define the condition has the potential to change the lives of the 750,000 adult Americans who suffer from it," said Dong-Jing Fu, MD, PhD, Director of Clinical Development at Janssen Scientific Affairs, LLC. "Janssen is proud to expand treatment options for those living with schizoaffective disorder and to provide new possibilities for the family members and friends who care for them."

Few large, controlled studies have systematically studied the clinical characteristics of schizoaffective disorder and long-term treatment options. This study, which included a 6-month open-label treatment period and a 15-month double-blind period, was the first registration trial to study maintenance treatment of a long-acting injectable in this complex disease. In addition to the approval of INVEGA® SUSTENNA® as monotherapy for schizoaffective disorder, it is approved as adjunctive therapy to mood stabilizers or antidepressants.

The most common INVEGA® SUSTENNA® adverse reactions, defined by at least a 5% incidence and twice that of placebo, are injection site reactions, somnolence/sedation, dizziness, akathisia and extrapyramidal disorder. No occurrences of these adverse events reached this threshold in this study of patients with schizoaffective disorder.

For additional study information, visit www.JanssenCNS.com.

About Schizoaffective Disorder

Schizoaffective disorder is a mental illness with an overlap of psychotic and mood symptoms. Psychotic symptoms include delusions or hallucinations, and mood symptoms include depression and mania. The exact cause of schizoaffective disorder is unknown. The disorder is diagnosed via a mental health assessment of symptoms over an extended period of time conducted by a licensed mental health professional. The full constellation of symptoms and the relevant diagnostic criteria should be consulted and are available in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5 or current version). Schizoaffective disorder is a complex condition that is generally treated with a combination of medications. In 2009, INVEGA®, another product manufactured by Janssen, became the first atypical antipsychotic approved to treat schizoaffective disorder. Other than INVEGA® (paliperidone) and INVEGA® SUSTENNA® (paliperidone palmitate), there are no antipsychotic medications indicated to treat this disorder in the U.S. or most other countries, and no widely accepted guidelines for the treatment of the disease are available.

About Janssen Pharmaceuticals, Inc.

As a member of the Janssen Pharmaceutical Companies of Johnson & Johnson, Janssen Pharmaceuticals, Inc., is dedicated to addressing and resolving the major unmet medical needs of our time. Driven by our commitment to patients, healthcare professionals, and caregivers, we strive to develop sustainable and integrated healthcare solutions by working in partnership with all stakeholders on the basis of trust and transparency. Our daily work is guided by meeting goals of excellence in quality, innovation, safety, and efficacy in order to advance patient care.

Our company provides medicines for an array of illnesses and disorders in several therapeutic areas. For more information on Janssen Pharmaceuticals, Inc., visit us at www.JanssenPharmaceuticalsInc.com or follow us on Twitter at www.Twitter.com/JanssenUS and on YouTube at www.YouTube.com/JanssenUS.

INVEGA® SUSTENNA® (paliperidone palmitate) is indicated for the treatment of:

- Schizophrenia.
- Schizoaffective disorder as monotherapy and as an adjunct to mood stabilizers or antidepressants.

IMPORTANT SAFETY INFORMATION FOR INVEGA® SUSTENNA® (paliperidone palmitate)

WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS.

See full Prescribing Information for complete Boxed Warning

- Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death.
- INVEGA® SUSTENNA® is not approved for the treatment of patients with dementia-related psychosis.

Contraindications: Paliperidone is contraindicated in patients with a known hypersensitivity to either paliperidone, risperidone, or to any excipients of the formulation.

Cerebrovascular Adverse Reactions: Cerebrovascular adverse reactions (e.g., stroke, transient ischemic attacks), including fatalities, were reported in placebo-controlled trials in elderly patients with dementia-related psychosis taking oral risperidone, aripiprazole, and olanzapine. The incidence of cerebrovascular adverse reactions was significantly higher than with placebo. INVEGA® SUSTENNA® 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 paliperidone. 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 close medical monitoring, and treatment of any concomitant serious medical problems.

QT Prolongation: Paliperidone causes a modest increase in the corrected QT (QTc) interval. Avoid the use of drugs that also increase QTc interval and in patients with risk factors for prolonged QTc interval. Paliperidone should also be avoided in patients with congenital long QT syndrome and in patients with a history of cardiac arrhythmias. Certain circumstances may increase the risk of the occurrence of torsades de pointes and/or sudden death in association with the use of drugs that prolong the QTc interval.

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, but can develop after relatively brief treatment at low doses. Elderly female patients appeared to be at increased risk for TD, although it is impossible to predict which patients will develop the syndrome. Prescribing should be consistent with the need to minimize the risk of TD (see full Prescribing Information). Discontinue drug if clinically appropriate. The syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn.

Metabolic Changes: Atypical antipsychotic drugs have been associated with metabolic changes that may increase cardiovascular/cerebrovascular risk. These metabolic changes include hyperglycemia, dyslipidemia, and body weight gain. While all of the drugs in the class have been shown to produce some metabolic changes, each drug has its own specific risk profile.

Hyperglycemia and Diabetes Mellitus: Hyperglycemia and diabetes mellitus, in some cases extreme and associated with ketoacidosis, hyperosmolar coma or death, have been reported in patients treated with all atypical antipsychotics (APS). Patients starting treatment with APS who have or are at risk for diabetes mellitus should undergo fasting blood glucose testing at the beginning of and during treatment. Patients who develop symptoms of hyperglycemia during treatment should also undergo fasting blood glucose testing. All patients treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia. Some patients require continuation of antidiabetic treatment despite discontinuation of the suspect drug.

Dyslipidemia: Undesirable alterations have been observed in patients treated with atypical antipsychotics.

Weight Gain: Weight gain has been observed with atypical antipsychotic use. Clinical monitoring of weight is recommended.

Orthostatic Hypotension and Syncope: INVEGA® SUSTENNA® may induce orthostatic hypotension in some patients due to its alpha-blocking activity. INVEGA® SUSTENNA® should be used with caution in patients with known cardiovascular disease, cerebrovascular disease or conditions that would predispose patients to hypotension (e.g., dehydration, hypovolemia, treatment with antihypertensive medications). Monitoring should be considered in patients for whom this may be of concern.

Leukopenia, Neutropenia and Agranulocytosis have been reported with antipsychotics, including paliperidone. Patients with a history of clinically significant low white blood cell count (WBC) or drug-induced leukopenia/neutropenia should have frequent complete blood cell counts during the first few months of therapy. At the first sign of a clinically significant decline in WBC, and in the absence of other causative factors, discontinuation of INVEGA® SUSTENNA® should be considered. Patients with clinically significant neutropenia should be carefully monitored for fever or other symptoms or signs of infection and treated promptly if such symptoms or signs occur. Patients with severe neutropenia (absolute neutrophil count < 1000/mm³) should discontinue INVEGA® SUSTENNA® and have their WBC followed until recovery.

Hyperprolactinemia: As with other drugs that antagonize dopamine D₂ receptors, INVEGA® SUSTENNA® elevates prolactin levels, and the elevation persists during chronic administration. Paliperidone has a prolactin-elevating effect similar to risperidone, which is associated with higher levels of prolactin elevation than other antipsychotic agents.

Potential for Cognitive and Motor Impairment: Somnolence, sedation, and dizziness were reported as adverse reactions in subjects treated with INVEGA® SUSTENNA®. INVEGA® SUSTENNA® has the potential to impair judgment, thinking, or motor skills. Patients should be cautioned about performing activities that require mental alertness such as operating hazardous machinery, including motor vehicles, until they are reasonably certain that INVEGA® SUSTENNA® does not adversely affect them.

Seizures: INVEGA® SUSTENNA® should be used cautiously in patients with a history of seizures or with conditions that potentially lower seizure threshold. Conditions that lower seizure threshold may be more prevalent in patients 65 years or older.

Administration: For intramuscular injection only by a healthcare professional. Care should be taken to avoid inadvertent injection into a blood vessel.

Drug Interactions: Strong CYP3A4/P-glycoprotein (P-gp) inducers: It may be necessary to increase the dose of INVEGA® SUSTENNA® when a strong inducer of both CYP3A4 and P-gp (e.g. carbamazepine, rifampin, St. John's wort) is co-administered. Conversely, on discontinuation of the strong inducer, it may be necessary to decrease the dose of INVEGA® SUSTENNA®.

Pregnancy/Nursing: Patients should be advised to notify their physician if they become pregnant/intend to become pregnant or intend to nurse during treatment with INVEGA® SUSTENNA®.

Commonly Observed Adverse Reactions for INVEGA® SUSTENNA®: The most common adverse reactions in clinical trials in patients with schizophrenia (≥5% and twice placebo) were injection site reactions, somnolence/sedation, dizziness, akathisia and extrapyramidal disorder. No adverse events occurred at a rate of ≥5% and twice placebo during the long-term double-blind, placebo-controlled study in patients with schizoaffective disorder. The following adverse reactions occurred more frequently (a ≥2% difference vs. placebo) in the long-term study in patients with schizoaffective disorder: weight increased, nasopharyngitis, headache, hyperprolactinemia, and pyrexia.

Please see full Prescribing Information including Boxed Warning for INVEGA® SUSTENNA® (paliperidone palmitate) and INVEGA® (paliperidone) at www.JanssenCNS.com/InvegaSustenna and www.JanssenCNS.com/Invega.

(This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding approval of a new indication. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Janssen Pharmaceuticals, Inc., Janssen Scientific Affairs, LLC, and/or Johnson & Johnson. Risks and uncertainties include, but are not limited to: uncertainty of commercial success; competition, including technological advances, new products and patents attained by competitors; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns or financial distress of purchasers of health care products and services; changes to laws and regulations, including domestic and foreign health care reforms; and general industry conditions, including trends toward health care cost containment. A further list and description of these risks, uncertainties and other factors can be found in Johnson & Johnson's Annual Report on Form 10-K for the fiscal year ended December 29, 2013, including in Exhibit 99 thereto, and the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov, www.jnj.com or on request from Johnson & Johnson. None of the Janssen Pharmaceutical Companies or Johnson & Johnson undertakes to update any forward-looking statement as a result of new information or future events or developments).

Media Contact:

Robyn Frenze
609-730-3468 (office)
215-370-7322 (mobile)

Investor Contacts:

Louise Mehrotra
732-524-6491 (office)

Stan Panasewicz
732-524-2524 (office)

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