Jazz Pharmaceuticals Announces U.S. Commercial Availability Of Versacloz™ (clozapine, USP) Oral Suspension

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First liquid formulation clozapine for treatment-resistant schizophrenia

DUBLIN, Feb. 11, 2014 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced U.S. commercial availability of Versacloz™ (clozapine, USP) oral suspension, the first and only oral suspension clozapine for severely ill treatment-resistant schizophrenia patients or those at risk of recurrent suicidal behavior with schizophrenia or schizoaffective disorder.

"We are pleased to offer patients with treatment-resistant schizophrenia a new liquid formulation of clozapine that is FDA approved to treat this difficult condition," said Bruce C. Cozadd, chairman and CEO at Jazz Pharmaceuticals plc. "Versacloz is an important addition to our existing psychiatry product portfolio and offers physicians another treatment option to help patients with limited treatment options."

Versacloz is an atypical antipsychotic indicated for the treatment of people with schizophrenia who have failed to respond adequately to other therapies.[1] Versacloz is also approved to reduce the risk of recurrent suicidal behavior in people with schizophrenia or schizoaffective disorder who are at chronic risk for re-experiencing suicidal behavior.[1] Versacloz has a unique, tasteless formulation and can be administered in an outpatient setting or under the supervision of a healthcare professional through an oral suspension. This formulation helps eliminate the mixing and matching of pill dosage strengths. In institutional settings, the formulation may help with confirmation of administration, and may reduce the possibility of "cheeking," hiding, or sharing the medication.

Because of the risk of agranulocytosis with clozapine therapy, Versacloz will be available only through a restricted program called the Versacloz Patient Registry, which ensures appropriate monitoring of white blood cell and absolute neutrophil count prior to delivery of the next refill of medication.[1] As part of its ongoing commitment to the psychiatry community, Jazz Pharmaceuticals, through the Versacloz Patient Registry and experienced Clinical Compliance Liaisons, will provide blood monitoring and reporting support services not typically offered by generic clozapine manufacturers.

"In my experience, some treatment-resistant schizophrenia patients may cycle through four or five typical and atypical antipsychotic treatments while failing to maintain adequate symptom control," said Gustavo Alva, MD, DFAPA, Medical Director at ATP Clinical Research. "When patients reach this stage, the next move matters – now with oral suspension Versacloz, we have another option to help patients."

The Food and Drug Administration (FDA) approval of Versacloz was based on general studies related to clozapine. Efficacy in treatment-resistant schizophrenia was established in a six-week active-controlled study in patients who had failed other antipsychotics. Efficacy in reducing recurrent suicidal behavior in patients with schizophrenia or schizoaffective disorder was demonstrated over a two-year treatment period in the InterSePT™ trial. As part of the New Drug Application filing for Versacloz, the FDA required a post-approval usability study to determine a patient's ability to self-administer the oral suspension.

Versacloz is distributed by Jazz Pharmaceuticals, Inc., a U.S. subsidiary of Jazz Pharmaceuticals plc.

INDICATION[1]
Versacloz is indicated for:

- Treatment-resistant schizophrenia in severely ill patients. Because of the significant risk of agranulocytosis and seizure associated with its use, Versacloz should be used only in patients who have failed to respond adequately to standard antipsychotic treatment. Efficacy was established in a 6-week, randomized, double-blind, active-controlled study comparing clozapine and chlorpromazine in patients who had failed other antipsychotics.
- Reduction in the risk of recurrent suicidal behavior in patients with schizophrenia or schizoaffective disorder at chronic risk for re-experiencing suicidal behavior, based on history and recent clinical state. Efficacy was demonstrated over a two-year treatment period in the InterSePT™ trial.

BOXED WARNING IMPORTANT SAFETY INFORMATION

Agranulocytosis: Clozapine has caused agranulocytosis, which can lead to serious infection and death. Monitor white blood cell count (WBC) and absolute neutrophil count (ANC) prior to and during treatment with VERSACLOZ. The ANC must be ≥ 2000/mm3 and the WBC must be ≥ 3500/mm3 for a patient to begin treatment. During treatment, discontinue and do not rechallenge if the ANC is < 1000/mm3 or the WBC is < 2000/mm3. Advise patients to immediately report symptoms consistent with agranulocytosis or infection (e.g., fever, weakness, lethargy, or sore throat).

Because of the risk of agranulocytosis, VERSACLOZ is available only through a restricted program called the VERSACLOZ Patient Registry. Prescribers, patients, and pharmacies must enroll in this restricted program. Further information is available at http://www.versaclozregistry.com or 1-877-329-2256.

Orthostatic Hypotension, Bradycardia, Syncope: Orthostatic hypotension, bradycardia, syncope, and cardiac arrest have occurred with clozapine treatment. Highest risk is during initial titration, particularly with rapid dose escalation and can occur with the first dose (12.5 mg/day). Titrate slowly and use divided dosages. Use VERSACLOZ cautiously in patients with cardiovascular/cerebrovascular disease or conditions predisposing to hypotension (e.g., dehydration, use of antihypertensive medications).

Seizures: Seizures have occurred with clozapine treatment. The risk is dose-related. Initiate treatment at 12.5 mg, titrate gradually, and use divided dosing. Use cautiously in patients with a history of seizures or predisposing risk factors (CNS pathology, medications that lower the seizure threshold, alcohol abuse). Caution patients about engaging in any activity where sudden loss of consciousness could cause serious risk to themselves or others.

Myocarditis and Cardiomyopathy: Fatal myocarditis and cardiomyopathy have occurred with clozapine treatment. Discontinue and obtain a cardiac evaluation upon suspicion of these reactions. Generally, patients with VERSACLOZ-related myocarditis or cardiomyopathy should not be rechallenged. Consider the possibility of myocarditis or cardiomyopathy if chest pain, tachycardia, palpitations, dyspnea, fever, flu-like symptoms, hypotension, or ECG changes occur.

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. VERSACLOZ is not approved for this condition.

- Contraindications include:[1]
  - History of clozapine-induced agranulocytosis or severe granulocytopenia
  - Known hypersensitivity to clozapine or any other component of VERSACLOZ
- Eosinophilia has occurred, usually during the first month of treatment with clozapine. In clinical trials, approximately 1% of patients developed eosinophilia. Discontinue VERSACLOZ if organ involvement (e.g., myocarditis, pancreatitis, hepatitis, colitis, nephritis) occurs.[1]
- QT interval prolongation, sometimes life-threatening, has occurred with clozapine. Consider additional risk factors for prolonged QT interval (disorders and drugs) including patient and family history, treatment with other medications that cause QT prolongation or inhibit the metabolism of VERSACLOZ and electrolyte abnormalities. Discontinue use if the QTc interval exceeds 500 msec or if the patient experiences symptoms consistent with Torsades de Pointes or other arrhythmias, (e.g., syncope, presyncope, dizziness, or palpitations).[1]
- Atypical antipsychotics, including clozapine have been associated with metabolic changes, including:[1]
  - Hyperglycemia and Diabetes Mellitus: Hyperglycemia, in some cases extreme associated with ketoacidosis and hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics including clozapine. Monitor for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Monitor glucose regularly in patients with or at risk for diabetes.
  - Dyslipidemia: Undesirable alterations in lipids have occurred in patients treated with atypical antipsychotics. Baseline and periodic follow-up lipid evaluations are recommended.
  - Weight Gain: Weight gain has occurred in clinical trials with clozapine. Monitor weight during treatment.
- Neuroleptic Malignant Syndrome (NMS), a potentially fatal symptom complex, has been reported with administration of antipsychotics, including clozapine. Clinical manifestations include hyperpyrexia, muscle rigidity, altered mental status and autonomic instability. Additional signs may include elevated creatine phosphokinase, myoglobinuria, rhabdomyolysis, and acute renal failure. If NMS occurs, immediately discontinue VERSACLOZ, manage with intensive symptomatic treatment, monitor closely, and assess for comorbidities.[1]
- Patients have experienced transient, clozapine-related fever during therapy, often within the first 3 weeks of treatment. Evaluate patients with fever for agranulocytosis, infection, or NMS.[1]
- Consider pulmonary embolism (PE) if respiratory distress, chest pain, or deep vein thrombosis occur.[1]
- CNS and peripheral anticholinergic toxicity can occur with VERSACLOZ. Use cautiously in the presence of narrow-angle glaucoma, concomitant anticholinergic drugs, prostatic hypertrophy, or other conditions in which anticholinergic effects can lead to significant adverse reactions.[1]
- Advise caution when operating machinery, including automobiles. Consider reducing the dose if cognitive or motor interference occurs.[1]
- Warnings and precautions also include the risk of tardive dyskinesia, caution in patients with risk factors for cerebrovascular adverse reactions and the need to monitor for recurrence of psychosis and cholinergic rebound after abrupt discontinuation of VERSACLOZ.[1]
- Common adverse reactions (>5%) across clozapine clinical trials were: CNS reactions, (sedation, dizziness/vertigo, headache, and tremor); cardiovascular reactions (tachycardia, hypotension, and syncope); autonomic nervous system reactions, (hypersalivation, sweating, dry mouth, and visual disturbances); gastrointestinal reactions, (constipation and nausea); and fever.[1]

Please click here to see the full Prescribing Information for important information about Versacloz, including BOXED Warning.

About Jazz Pharmaceuticals

Jazz Pharmaceuticals plc is a specialty biopharmaceutical company focused on improving patients' lives by identifying, developing and commercializing innovative products that address unmet medical needs. The company has a diverse portfolio of products in the areas of narcolepsy, hematology/oncology, pain and psychiatry. The company's U.S. marketed products in these areas include: Xyrem® (sodium oxybate) oral solution, Erwinaze® (asparaginase Erwinia chrysanthemi), Prialt® (ziconotide) intrathecal infusion, Versacloz™ (clozapine, USP) oral suspensions, FazaClo® (clozapine, USP) HD and FazaClo LD. Jazz Pharmaceuticals also has a number of products marketed outside the U.S. and expects to launch Defitelio™ (defibrotide) in the European Union over the course of 2014. The company has product candidates in development in its sleep and hematology/oncology franchises. For further information, see www.jazzpharmaceuticals.com.

"Safe Harbor" Statement under the Private Securities Litigation Reform Act of 1995
This press release contains forward-looking statements, including, but not limited to, statements related to the therapeutic and commercial potential of Versacloz, the expected launch of Defitelio in the European Union and the timing thereof, and other statements that are not historical facts. These forward-looking statements are based on Jazz Pharmaceuticals' current expectations and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks and uncertainties associated with the possibility that the company may fail to realize the anticipated benefits from Versacloz; the company's ability to successfully launch and commercialize Defitelio in a timely manner; the company's ability to successfully manage the risks associated with integrating Defitelio and any other products or product candidates the company may acquire in the future into the company's product portfolio; as well as risks related to future opportunities and plans; and those other risks detailed from time-to-time under the caption "Risk Factors" and elsewhere in Jazz Pharmaceuticals plc's Securities and Exchange Commission filings and reports (Commission File No. 001-33500), including the Quarterly Report on Form 10-Q for the quarter ended September 30, 2013 and future filings and reports by the company. Jazz Pharmaceuticals undertakes no duty or obligation to update any forward-looking statements contained in this press release as a result of new information, future events or changes in its expectations.

References:

1. Versacloz™ Prescribing Information. Palo Alto, CA. Jazz Pharmaceuticals. 2013.

SOURCE Jazz Pharmaceuticals plc

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