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BRIEF SUMMARY of Prescribing Information—Before prescribing, please consult complete Prescribing Information.

Increased Mortality in Elderly Patients with Dementia-Related Psychosis

Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks) in these patients revealed a risk of death in the drug-treated patients between 1.6 to 1.7 times that seen 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 (eg, heart failure, sudden death) or infectious (eg, pneumonia) in nature. SEROQUEL (quetiapine) is not approved for the treatment of patients with Dementia-Related Psychosis.

WARNINGS: Increased Mortality in Elderly Patients with Dementia-Related Psychosis: Elderly patients with dementia-related psychosis treated with atypical antipsychotic drugs are at an increased risk of death compared to placebo. SEROQUEL (quetiapine) is not approved for the treatment of patients with dementia-related psychosis (see Boxed Warning). **Neuroleptic Malignant Syndrome (NMS):** A potentially fatal symptom complex sometimes has been reported to occur with neuroleptic drugs. Signs and symptoms of NMS include hyperreflexia and autonomic dysfunction. SEROQUEL has been associated with NMS. Elderly patients with dementia-related psychosis treated with SEROQUEL have reported with SEROQUEL. Clinical manifestations of NMS are hyperreflexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (myoglobinuria) and acute renal failure. The diagnostic evaluation of patients with this syndrome is complicated. In arriving at a diagnosis, it is important to exclude causes other than NMS. Information obtained from the patient's history, physical examination, and laboratory data is helpful. In the absence of a clear alternative diagnosis, NMS should be considered. The syndrome should be treated with the following: 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy; 2) intensive symptomatic treatment and medical monitoring, and treatment of any concomitant serious medical problems for which specific treatments are available. There is no general consensus about specific treatment approaches. In some cases, a patient requires antipsychotic drug treatment after recovery from NMS; the potential reintroduction of drug therapy should be carefully considered. The patient should be carefully monitored since recurrences of NMS have been reported. **Tardive Dyskinesia:** A syndrome of potentially irreversible, involuntary, dyskinetic movements may develop in patients treated with antipsychotic drugs. Although the prevalence of the syndrome appears to be highest among the elderly, especially elderly women, it is impossible to rely upon prevalence estimates to predict, at the inception of antipsychotic treatment, the risk that an individual will develop tardive dyskinesia. Once the syndrome has developed, it may become irreversible. Unfortunately, the risk of developing tardive dyskinesia and the likelihood that it will become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic drugs administered to the patient increase. However, the syndrome can develop, although less commonly, after relatively brief treatment periods at low doses. There is no known treatment for established cases of tardive dyskinesia although the syndrome may remit, partially or completely. If antipsychotic treatment is withdrawn, antipsychotic withdrawal symptoms may occur. However, because the syndrome may not develop until months after the last dose of an antipsychotic drug, the absence of the syndrome does not necessarily mean that it will not develop. The syndrome may be partially mask by the underlying process. The effect that symptomatic suppression has upon the long-term course of the syndrome is unknown. Given these considerations, SEROQUEL should be prescribed in a manner that is most likely to minimize the occurrence of tardive dyskinesia. Chronic antipsychotic treatment should generally be reserved for patients who appear to suffer from a chronic illness that (1) is known to respond to antipsychotic drugs, and (2) for whom alternative, effective, but potentially less harmful treatments are not available or appropriate. In addition, because the syndrome may develop after treatment is discontinued, patients who have received a satisfactory clinical response should be sought. The need for continued treatment should be reassessed periodically. If signs and symptoms of tardive dyskinesia appear in a patient on SEROQUEL, drug discontinuation should be considered. However, some patients may require treatment with SEROQUEL despite the presence of the syndrome.

Hyperglycemia and Diabetes Mellitus: Hyperglycemia, in some cases extreme and associated with ketotoxicosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics, including SEROQUEL. The relationship between the use of atypical antipsychotics and the development of hyperglycemia and the possibility of an increased background risk of diabetes mellitus in patients with schizophrenia and the increasing incidence of diabetes mellitus in the general population. Given these confounders, the relationship between atypical antipsychotic use and hyperglycemia-related adverse events is not completely understood. However, epidemiological studies suggest an increased risk of treatment-emergent hyperglycemia-related adverse events in patients treated with the atypical antipsychotics. Precise risk estimates for hyperglycemia-related adverse events in patients with atypical antipsychotics are not available. Therefore, patients at risk for hyperglycemia-related adverse events are started on atypical antipsychotics should be monitored regularly for worsening of glucose control. Patients with no risk factors for diabetes mellitus (age, obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of treatment and periodically during treatment. 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 during treatment with atypical antipsychotics should undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued. However, some patients may require ongoing diabetes-related treatment despite discontinuation of the suspected drug.

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