Dear Doctor,

Sunovion Pharmaceuticals Inc. has announced that Latuda® (lurasidone HCl) is ***now*** indicated for the treatment of patients with major depressive episodes associated with bipolar I disorder (bipolar depression) as monotherapy and as adjunctive therapy with lithium or valproate. LATUDA is also indicated for the treatment of patients with schizophrenia and is available as 20 mg, 40 mg, 80 mg, and 120 mg tablets. LATUDA has also recently received approval of a 60 mg strength tablet which will be available in October 2013.

In two studies in adult patients with bipolar depression, LATUDA was shown to be effective in a dose range of 20 mg/day to 120 mg/day. For the treatment of bipolar depression, the recommended starting dose of LATUDA is 20 mg given once daily as monotherapy or as adjunctive therapy with lithium or valproate. Initial dose titration is not required. The maximum recommended dose for the treatment of bipolar depression, as monotherapy or as adjunctive therapy with lithium or valproate, is 120 mg/day. In the monotherapy study that evaluated both a higher and a lower dose range of LATUDA, the higher dose range (80 to 120 mg/day) did not provide additional efficacy on average, compared to the lower dose range (20 to 60 mg/day). LATUDA should be taken with food (at least 350 calories). Please refer to the full Prescribing Information for dose modifications related to renal impairment, hepatic impairment, and concomitant use with CYP3A4 inhibitors and inducers. (Sections 2.4, 2.5).

The efficacy and safety of LATUDA for the treatment of bipolar depression as monotherapy was established in a 6-week, multicenter, randomized, double-blind, placebo-controlled study of adult patients (mean age of 41.5 years, range 18 to 74) who met DSM-IV-TR criteria for major depressive episodes associated with bipolar I disorder, with or without rapid cycling, and without psychotic features (N=485). Patients were randomized to flexibly dosed LATUDA 20 to 60 mg/day, LATUDA 80 to 120 mg/day, or placebo. The efficacy and safety as adjunctive therapy with lithium or valproate was established in a 6-week, multicenter, randomized, double-blind, placebo-controlled study of adult patients (mean age of 41.7 years, range 18 to 72) who met DSM-IV-TR criteria for major depressive episodes associated with bipolar I disorder, with or without rapid cycling, and without psychotic features (N=340). Patients who remained symptomatic after treatment with lithium or valproate were randomized to flexibly dosed LATUDA 20 to 120 mg/day or placebo. The primary rating instrument used to assess the severity of depressive symptoms in both studies was the Montgomery-Asberg Depression Rating Scale (MADRS). The primary endpoint was the change from baseline in MADRS score at Week 6. The key secondary instrument was the Clinical Global Impression-Bipolar-Severity of Illness scale (CGI-BP-S).

LATUDA was superior to placebo in reduction of MADRS and CGI-BP-S scores at Week 6 in both studies. In the monotherapy and adjunctive therapy studies, mean baseline MADRS scores were approximately 30 across all treatment groups. In the monotherapy study, the least-square mean change from baseline in the MADRS score was -15.4 in both the LATUDA treatment groups (20-60 mg/day and 80-120 mg/day) vs. -10.7 in the placebo group. In the adjunctive therapy study, the least-square mean change from baseline in the MADRS score was -17.1 in the LATUDA 20-120 mg/day + lithium or valproate group vs. -13.5 in the placebo + lithium or valproate group.

The most common adverse reactions (incidence ≥5% and at least twice the rate of placebo) in patients treated with LATUDA in the 6-week monotherapy study were akathisia, extrapyramidal symptoms, somnolence, nausea, vomiting, diarrhea, and anxiety; and in patients treated with LATUDA in the 6-week adjunctive therapy studies were akathisia and somnolence.

Please see Important Safety Information, including **Boxed Warnings**, below and click here for full Prescribing Information.

IMPORTANT SAFETY INFORMATION AND INDICATIONS FOR LATUDA

WARNINGS:

INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA RELATED PSYCHOSIS; AND SUICIDAL THOUGHTS AND BEHAVIORS

- **Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. LATUDA is not approved for use in patients with dementia-related psychosis.**
- **Antidepressants increased the risk of suicidal thoughts and behavior in children, adolescents, and young adults in short-term studies. These studies did not show an increase in the risk of suicidal thoughts and behavior with antidepressant use in patients over age 24; there was a reduction in risk with antidepressant use in patients aged 65 and older. In patients of all ages who are started on antidepressant therapy, monitor closely for worsening, and for emergence of suicidal thoughts and behaviors. Advise families and caregivers of the need for close observation and communication with the prescriber. LATUDA is not approved for use in patients under the age of 18 years.**

CONTRAINDICATIONS

LATUDA is contraindicated in the following:

- Known hypersensitivity to lurasidone HCl or any components in the formulation. Angioedema has been observed with lurasidone.
- Strong CYP3A4 inhibitors (e.g., ketoconazole)
- Strong CYP3A4 inducers (e.g., rifampin)

WARNINGS AND PRECAUTIONS

Cerebrovascular Adverse Reactions, Including Stroke: In placebo-controlled trials with risperidone, aripiprazole, and olanzapine in elderly subjects with dementia, there was a higher incidence of cerebrovascular adverse reactions (cerebrovascular accidents and transient ischemic attacks) including fatalities compared to placebo-treated subjects. LATUDA 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 administration of antipsychotic drugs, including LATUDA. NMS can cause hyperpyrexia, 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 (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): TD is a syndrome consisting of potentially irreversible, involuntary, dyskinetic movements that can develop in patients with antipsychotic drugs. There is no known treatment for established cases of TD, although the syndrome may remit, partially or completely, if antipsychotic treatment is withdrawn. The risk of developing TD 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 much less commonly, after relatively brief treatment periods at low doses. Given these considerations, LATUDA should be prescribed in a manner that is most likely to minimize the occurrence of TD. If signs and symptoms appear in a patient on LATUDA, drug discontinuation should be considered.

Metabolic Changes

Hyperglycemia and Diabetes Mellitus: Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics. Patients with risk factors for diabetes mellitus (e.g., obesity, family history of diabetes) who are starting treatment with atypical antipsychotics should undergo fasting blood glucose testing at the beginning of 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 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.

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

Hyperprolactinemia: As with other drugs that antagonize dopamine D2 receptors, LATUDA elevates prolactin levels. Galactorrhea, amenorrhea, gynecomastia, and impotence have been reported in patients receiving prolactin-elevating compounds.

Leukopenia, Neutropenia, and Agranulocytosis: Leukopenia/neutropenia has been reported during treatment with antipsychotic agents. Agranulocytosis (including fatal cases) has been reported with other agents in the class. Patients with a preexisting low white blood cell count (WBC) or a history of drug-induced leukopenia/neutropenia should have their complete blood count (CBC) monitored frequently during the first few months of therapy, and LATUDA should be discontinued at the first sign of a decline in WBC in the absence of other causative factors.

Orthostatic Hypotension and Syncope: LATUDA may cause orthostatic hypotension. Orthostatic vital signs should be monitored in patients who are vulnerable to hypotension and in patients with known cardiovascular disease or cerebrovascular disease.

Seizures: LATUDA should be used cautiously in patients with a history of seizures or with conditions that lower seizure threshold (e.g., Alzheimer's dementia).

Potential for Cognitive and Motor Impairment: Patients should be cautioned about operating hazardous machinery, including motor vehicles, until they are reasonably certain that therapy with LATUDA does not affect them adversely.

Body Temperature Regulation: Disruption of the body's ability to reduce core body temperature has been attributed to antipsychotic agents. Appropriate care is advised when prescribing LATUDA for patients who will be experiencing conditions that may contribute to an elevation in core body temperature, e.g., exercising strenuously, exposure to extreme heat, receiving concomitant medication with anticholinergic activity, or being subject to dehydration.

Suicide: The possibility of suicide attempt is inherent in psychotic illness and close supervision of high-risk patients should accompany drug therapy. Prescriptions for LATUDA should be written for the smallest quantity of tablets 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. Aspiration pneumonia is a common cause of morbidity and mortality in elderly patients, in particular those with advanced Alzheimer's dementia. LATUDA and other antipsychotic drugs should be used cautiously in patients at risk for aspiration pneumonia.

ADVERSE REACTIONS

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

- Adult patients with bipolar depression: akathisia, extrapyramidal symptoms, and somnolence
- Adult patients with schizophrenia: somnolence, akathisia, extrapyramidal symptoms, and nausea

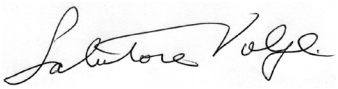
INDICATIONS

LATUDA is indicated for:

- Treatment of major depressive episodes associated with bipolar I disorder (bipolar depression) as monotherapy and as adjunctive therapy with lithium or valproate in adults
- Treatment of schizophrenia in adults

Before prescribing LATUDA, please read the enclosed full Prescribing Information, including **Boxed Warnings**.

Respectfully,



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