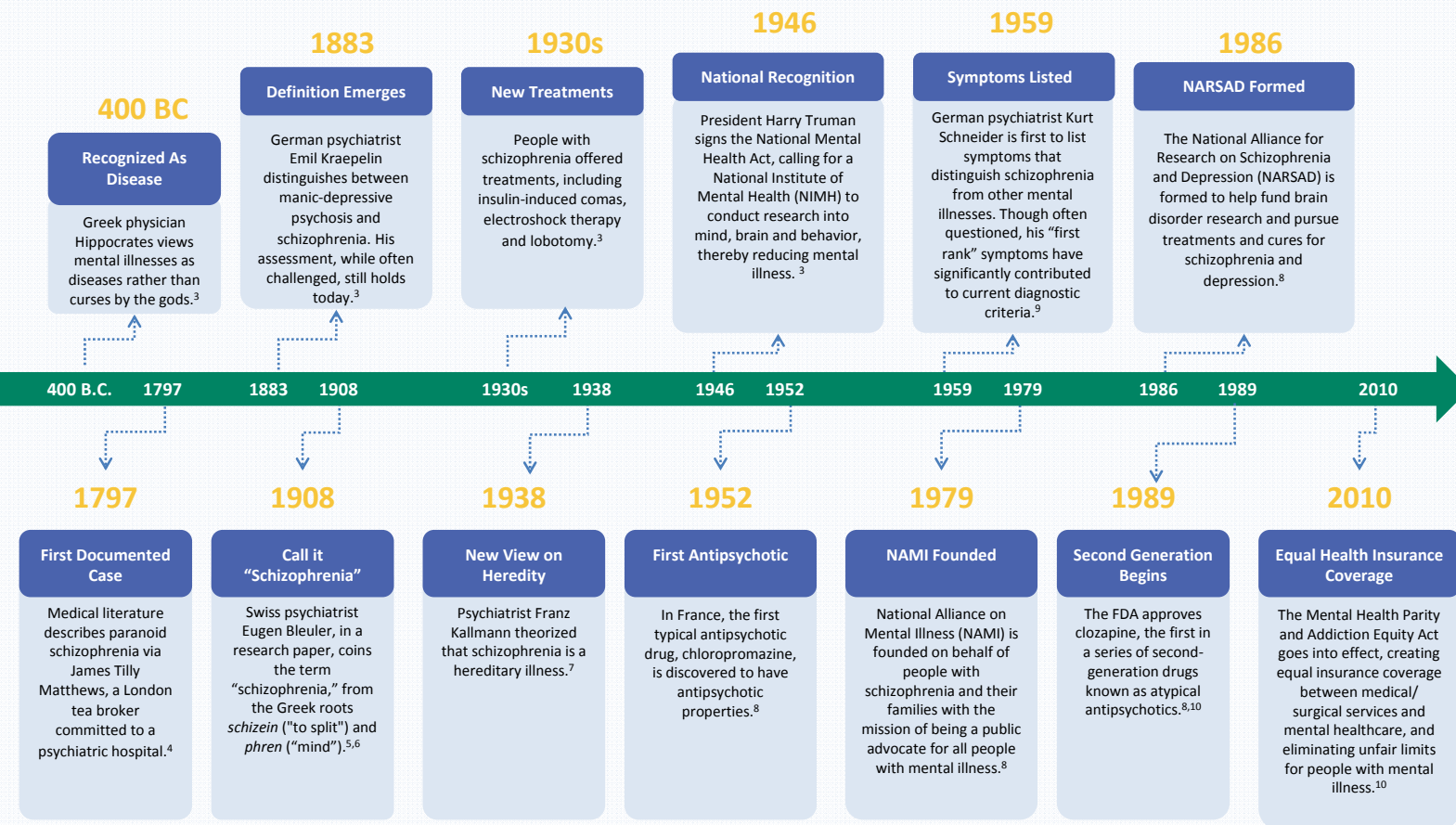


# HISTORY OF SCHIZOPHRENIA



\* Schizophrenia is a chronic, disabling and serious brain disorder that affects approximately 2.4 million American adults or 1 in 100 people.<sup>1</sup> Schizophrenia is characterized by symptoms such as hallucinations, delusions, disorganized thinking, lack of emotion, lack of energy, as well as problems with memory, attention and the ability to plan, organize and make decisions.<sup>2</sup>



## LATUDA Milestones

- 1990s: Scientists at Dainippon Sumitomo Pharma Co. Ltd. (DSP) develop lurasidone molecule and initiate studies
- November 1995: First study in humans in Japan
- May 2009: Data from pivotal PEARL 1 study results announced
- August 2009: Data from pivotal PEARL 2 study results announced
- December 2009: New Drug Application (NDA) submitted to the U.S. Food and Drug Administration (FDA)
- October 2010: FDA approves LATUDA for the treatment of patients with schizophrenia
- February 2011: LATUDA is made available by prescription in pharmacies across the United States and Puerto Rico

## Company Fast Facts

LATUDA represents Sunovion Pharmaceuticals Inc.'s first FDA approval since becoming the U.S. subsidiary of DSP

DSP is one of the few companies to develop in-house three atypical antipsychotics – two of which are available in Asia

LATUDA is DSP's third atypical antipsychotic compound and its first product marketed in the U.S.

**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 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 (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. LATUDA is not approved for the treatment of patients with dementia-related psychosis.

Please see Important Safety Information, including **Boxed Warning** below, and full Prescribing Information at [www.LATUDA.com](http://www.LATUDA.com).

## About LATUDA

LATUDA is an atypical antipsychotic indicated for the treatment of patients with schizophrenia. Efficacy was established in four 6-week controlled studies of adult patients with schizophrenia. The effectiveness of LATUDA for longer-term use, that is, for more than 6 weeks, has not been established in controlled studies. Therefore, the physician who elects to use LATUDA for extended periods should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

## Dosage and Administration

The recommended dose for LATUDA is 40mg/day taken with food (at least 350 calories) with no initial dose titration required. The maximum recommended dose is 80 mg/day. For patients with moderate to severe renal or hepatic impairment, the dose of LATUDA should not exceed 40 mg/day. LATUDA should not be administered with strong CYP3A4 inhibitors such as ketoconazole or strong CYP3A4 inducers such as rifampin.

## IMPORTANT SAFETY INFORMATION FOR LATUDA

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

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## CONTRAINDICATIONS

LATUDA is contraindicated in any patient with a known hypersensitivity to lurasidone HCl or any components in the formulation. Angioedema has been observed with lurasidone. LATUDA is contraindicated with strong CYP3A4 inhibitors (e.g., ketoconazole) and 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. The management of NMS should include: 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy; 2) intensive symptomatic treatment and medical monitoring; and 3) treatment of any concomitant serious medical problems for which specific treatments are available.

**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. In short-term, placebo-controlled studies, the increase in prolactin was greater in LATUDA-treated female patients; the median change from baseline to endpoint for females was 1.5 ng/mL and was 1.1 ng/mL in males. The increase in prolactin concentrations was dose-dependent. The proportion of female patients with prolactin elevations  $\geq 5 \times$  ULN was 8.3% for LATUDA-treated patients versus 1% for placebo-treated female patients. The proportion of male patients with prolactin elevations  $> 5 \times$  ULN was 1.9% versus 0.6% for placebo-treated male patients.

**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. LATUDA should be used with caution in patients with known cardiovascular disease (e.g., heart failure, history of myocardial infarction, ischemia, or conduction abnormalities), cerebrovascular disease, or conditions that predispose the patient to hypotension (e.g., dehydration, hypovolemia, and treatment with antihypertensive medications). Monitoring of orthostatic vital signs should be considered in all patients who are vulnerable to hypotension.

**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:** In short-term, placebo-controlled trials, somnolence was reported in 22.3% (224/1004) of patients treated with LATUDA compared to 9.9% (45/455) of placebo patients, respectively. The frequency of somnolence increases with dose. 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 is not indicated for the treatment of dementia-related psychosis, and should not be used in patients at risk for aspiration pneumonia.

## DRUG INTERACTIONS

**Drug Interactions:** Given the primary CNS effects of LATUDA, caution should be used when it is taken in combination with other centrally acting drugs and alcohol.

## ADVERSE REACTIONS

**Commonly Observed Adverse Reactions** ( $\geq 5\%$  and at least twice that for placebo): The most commonly observed adverse reactions in patients treated with LATUDA in short-term clinical studies were somnolence, akathisia, nausea, parkinsonism, and agitation.

Please see Full Prescribing Information, including **Boxed Warning**, on [www.LATUDA.com](http://www.LATUDA.com).

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