Metabolic Changes: Atypical antipsychotic drugs have been associated with metabolic changes that include:

- **Hyperglycemia/Diabetes Mellitus**: Hyperglycemia, in some cases extreme and associated with ketoacidosis, coma, or death, has been reported in patients treated with atypical antipsychotics. There have been reports of hyperglycemia in patients treated with oral aripiprazole. Patients with diabetes should be regularly monitored for worsening of glucose control; those with risk factors for diabetes should undergo baseline and periodic fasting blood glucose testing. 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 should also undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients require continuation of antidiabetic 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 antipsychotics. Clinical monitoring of weight is recommended.

Pathological Gambling and Other Compulsive Behaviors: Compulsive or uncontrollable urges to gamble have been reported with use of aripiprazole. Other compulsive urges less frequently reported include binge eating, increased gambling, shopping, binging and eating, and other impulsive or compulsive behaviors which may result in harm for the patient and others if not recognized. Closely monitor patients and consider dose reduction or stopping aripiprazole if a patient develops such urges.

Orthostatic Hypotension: Aripiprazole may cause orthostatic hypotension which can be associated with dizziness, lightheadedness, and tachycardia. Monitor heart rate and blood pressure, and warn patients with known cardiovascular or cerebrovascular disease of the risk of dehydration and syncope.

Dystonia: Symptoms of dystonia, prolonged muscle stiffness, are reported with antipsychotic use. Injection-site reactions were reported by 4%, 5%, and/or ARISTADA INITIO were reported by 5%, 5%, and at least 1% of patients taking ARISTADA INITIO and/or ARISTADA during pregnancy. Aripiprazole is not approved for the treatment of patients with dementia-related psychosis.

Potential for Dosing and Medication Errors: Medication errors, including substitution and dispensing errors, between ARISTADA INITIO and ARISTADA could occur. ARISTADA INITIO is intended for single administration only. Do not substitute ARISTADA INITIO for ARISTADA because of differing pharmacokinetic profiles.

Neuroleptic Malignant Syndrome (NMS): A potentially fatal or life-threatening complex may occur with administration of antipsychotic drugs, including ARISTADA INITIO and ARISTADA. Clinical manifestations of NMS include hyperpyrexia, muscle rigidity, altered mental status, autonomic instability (irregular pulse or blood pressure), altered cardiovascular and cerebrovascular disease risk and risk of dehydration and syncope.

Falls: Antipsychotics including ARISTADA INITIO and ARISTADA may cause somnolence, postural hypotension and motor and sensory instability which may lead to falls and subsequent injury. Upon initiating treatment and recurrently, complete fall assessments as appropriate.

Leukopenia, Neutropenia, and Agranulocytosis: Leukopenia, neutropenia and agranulocytosis have been reported with antipsychotics. Monitor complete blood counts and blood pressure, and warn patients with known hematologic problems of the risk of hematologic abnormalities.

Seizures: Use with caution in patients with a history of seizures or with conditions that lower the seizure threshold.

Potential for Cognitive and Motor Impairment: ARISTADA INITIO and ARISTADA may impair judgment, thinking, or motor skills. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are certain therapy with ARISTADA INITIO and/or ARISTADA do not affect them adversely.

Body Temperature Regulation: Disruption of the body’s ability to reduce core body temperature has been attributed to antipsychotic agents. Advise patients regarding appropriate care in avoiding overheating and dehydration. Appropriate care is advised for patients exercising strenuously, may be exposed to extreme heat, receive concomitant medication with anticholinergic activity, or are subject to dehydration.

**Dysphagia**: Esophageal dysmotility and aspiration have been associated with antipsychotic drug use. Use caution in patients at risk for aspiration pneumonia.

**Concomitant Medication**: ARISTADA INITIO is only available at a single strength as a single dose pre-filled syringe, so dosage adjustments are not possible. Avoid use in patients who are known CYP2D6 poor metabolizers or taking strong CYP3A4 inhibitors, strong CYP2D6 inhibitors, or strong CYP3A4 inducers, antihypertensive drugs or benzodiazepines.

Depending on the ARISTADA dose, adjustments should be made if patient is known CYP2D6 poor metabolizers and/or 2) taking CYP3A4 inhibitors, CYP2D6 inhibitors, or CYP3A4 inducers for greater than 2 weeks. Avoid use of ARISTADA 662 mg, 882 mg, or 1064 mg for patients taking both strong CYP3A4 inhibitors and strong CYP2D6 inhibitors. (See Table 4 in the ARISTADA full Prescribing Information.)

**Commonly Observed Adverse Reactions**: In pharmacokinetic studies the safety profile of ARISTADA INITIO was generally consistent with that observed for ARISTADA. The most common adverse reaction (≥5% incidence and at least twice the rate of placebo reported by patients treated with ARISTADA 441 mg and 882 mg) was akathisia.

**Injection-Site Reactions**: In pharmacokinetic studies evaluating ARISTADA INITIO, the incidences of injection-site reactions with ARISTADA INITIO were similar to the incidence observed with ARISTADA. Injection-site reactions were reported by 4%, 2%, and 2% of patients treated with 441 mg ARISTADA (monthly), 882 mg ARISTADA (monthly), and placebo, respectively. Most of these were injection-site pain and associated with the first injection and decreased with each subsequent injection. Other injection-site reactions (induration, swelling, and redness) occurred at less than 1%.

**Dystonia**: Symptoms of dystonia, prolonged abnormal contractions of muscle groups, may occur in susceptible individuals during the first days of treatment and at low doses.

**Pregnancy/Nursing**: May cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure. Advise patients to notify their healthcare provider of a known or suspected pregnancy. Inform patients that there is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to ARISTADA INITIO and/or ARISTADA during pregnancy. Aripiprazole is present in human breast milk. The benefits of breastfeeding should be considered along with the mother’s clinical need for ARISTADA INITIO and/or ARISTADA and any potential adverse effects on the infant from ARISTADA INITIO and/or ARISTADA or from the underlying maternal condition.