About ARISTADA™ (aripiprazole lauroxil) Extended-Release Injectable Suspension for the Treatment of Schizophrenia

Overview
ARISTADA™ (aripiprazole lauroxil) extended-release injectable suspension is a long-acting atypical antipsychotic that is approved by the U.S. Food and Drug Administration (FDA) for the treatment of schizophrenia. ARISTADA has demonstrated efficacy and safety, and provides healthcare professionals with a new long-acting injectable treatment option. Data from the package that supported the New Drug Application (NDA) filing showed that multiple dose strengths of ARISTADA administered once-monthly demonstrated statistically significant reductions in schizophrenia symptoms by change in total Positive and Negative Syndrome Scale (PANSS) score from baseline to Week 12, compared to placebo. The PANSS score is a thirty-item scale that measures symptoms of schizophrenia.

The product contains a Boxed Warning regarding the increased risk of mortality in elderly patients with dementia-related psychosis. ARISTADA is not approved for the treatment of patients with dementia-related psychosis. Please see below for additional Important Safety Information.

Product Attributes
ARISTADA is an atypical antipsychotic administered as a long-acting injectable medication for the treatment of schizophrenia. Tolerability with oral aripiprazole must be established before starting ARISTADA. In conjunction with the first ARISTADA injection, oral aripiprazole must be given for 21 consecutive days. Depending on the dose, ARISTADA has multiple options for dose strengths, dosing intervals and sites for administering the intramuscular (IM) injection in a pre-filled syringe. Specific product attributes include:

- Dosing strength options: 441 mg, 662 mg and 882 mg;
- Dosing interval options: once-monthly for all doses, and a once-every-six-weeks option available for the 882 mg dose;
- Location of IM administration: gluteus administration for all doses, with an option of deltoid administration for the 441 mg dose; and
- Available in a pre-filled syringe.

ARISTADA is a long-acting injectable medication, providing patients with blood concentrations of active antipsychotic drug that remain within a therapeutic range for a one month or six week period depending on the dose.

Please see accompanying full Prescribing Information, including Boxed Warning, and Medication Guide.
Key Clinical Data
The FDA approval of ARISTADA was based on proven safety and efficacy, including data from a randomized, double-blind, placebo-controlled, phase 3 study of aripiprazole lauroxil in patients with schizophrenia. Patients treated with ARISTADA in the study showed statistically significant reductions from baseline in PANSS total scores at Week 12, compared to placebo. The most common adverse reaction seen in the clinical trial was akathisia.

The phase 3 study results, “A Randomized, Double-Blind, Placebo-Controlled Trial of Aripiprazole Lauroxil in Acute Exacerbation of Schizophrenia,” were published in the Journal of Clinical Psychiatry in June 2015.

About Schizophrenia and Long-Acting Injectable Medicines
Schizophrenia is a chronic, severe and disabling brain disorder. The disease is marked by positive symptoms (hallucinations and delusions) and negative symptoms (depression, blunted emotions and social withdrawal), as well as by disorganized thinking. An estimated 2.4 million American adults have schizophrenia,1 with men and women affected equally. Worldwide, it is estimated that one person in every 100 develops schizophrenia, which is one of the most serious types of mental illness. Long-acting injectable antipsychotics offer an alternative treatment option to the daily dosing of oral antipsychotic medications and provide patients with blood concentrations of active drug that remain within a therapeutic range for an extended period of time.2

INDICATION and IMPORTANT SAFETY INFORMATION for ARISTADA™ (aripiprazole lauroxil) extended-release injectable suspension, for intramuscular use

INDICATION
ARISTADA is a prescription medicine given by injection by a healthcare professional and used to treat schizophrenia. It is not known if ARISTADA is safe and effective in children under 18 years of age.

IMPORTANT SAFETY INFORMATION

Elderly people with dementia-related psychosis are at increased risk of death when treated with antipsychotic medicines including ARISTADA. ARISTADA is not for the treatment of people who have lost touch with reality (psychosis) due to confusion and memory loss (dementia).

Contraindication: Do not receive ARISTADA if you are allergic to aripiprazole or any of the ingredients in ARISTADA. Allergic reactions to aripiprazole have ranged from rash, hives and itching to anaphylaxis, which may include difficulty breathing, tightness in the chest, and swelling of the mouth, face, lips, or tongue.

Please see accompanying full Prescribing Information, including Boxed Warning, and Medication Guide.
ARISTADA may cause serious side effects including:

- **Stroke in elderly people (cardiovascular problems) that can lead to death.**
- **Neuroleptic malignant syndrome (NMS) a serious condition that can lead to death.** Tell your healthcare provider right away if you have some or all of the following symptoms of NMS: high fever, stiff muscles, confusion, sweating, and changes in pulse, heart rate, and blood pressure. **Call your healthcare provider right away if you have any of these symptoms.**
- **Uncontrolled body movements (tardive dyskinesia).** ARISTADA may cause movements that you cannot control in your face, tongue, or other body parts. Tardive dyskinesia may not go away, even if you stop receiving ARISTADA. Tardive dyskinesia may also start after you stop receiving ARISTADA.
- **Problems with your metabolism such as:**
  - **High blood sugar (hyperglycemia):** Increases in blood sugar can happen in some people who take ARISTADA. Extremely high blood sugar can lead to coma or death. If you have diabetes or risk factors for diabetes (such as being overweight or a family history of diabetes), your healthcare provider should check your blood sugar before you start receiving ARISTADA and during your treatment.
    - **Call your healthcare provider if you have any of these symptoms of high blood sugar while receiving ARISTADA:**
      - feel very thirsty
      - need to urinate more than usual
      - feel very hungry
      - feel weak or tired
      - feel sick to your stomach
      - feel confused, or your breath smells fruity
    - **Increased fat levels (cholesterol and triglycerides) in your blood**
    - **Weight gain.** You and your healthcare provider should check your weight regularly.
  - **Decreased blood pressure (orthostatic hypotension).** You may feel lightheaded or faint when you rise too quickly from a sitting or lying position.
  - **Low white blood cell count**
  - **Seizures (convulsions)**
  - **Problems controlling your body temperature so that you feel too warm.** Do not become too hot or dehydrated while you receive ARISTADA. Do not exercise too much. In hot weather, stay inside in a cool place if possible. Stay out of the sun. Do not wear too much clothing or heavy clothing. Drink plenty of water.
  - **Difficulty swallowing**

The most common side effect of ARISTADA includes feeling like you need to move to stop unpleasant feelings in your legs (restless leg syndrome or akathisia).

Tell your healthcare provider if you have any side effect that bothers you or does not go away. You are encouraged to report all side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.
These are not all the possible side effects of ARISTADA. For more information, ask your healthcare provider or pharmacist.

Do not drive, operate machinery, or do other dangerous activities until you know how ARISTADA affects you. ARISTADA may make you feel drowsy.

Do not drink alcohol while you receive ARISTADA.

Tell your healthcare provider before receiving ARISTADA if you:

- have never taken any aripiprazole product before
- have diabetes or high blood sugar or a family history of diabetes or high blood sugar.
  Your healthcare provider should check your blood sugar before you start receiving ARISTADA and during your treatment.
- have or had seizures (convulsions)
- have or had low or high blood pressure
- have or had heart problems or a stroke
- have or had a low white blood cell count
- have any other medical problems including problems that may affect you receiving an injection in your buttocks or your arm
- are pregnant or plan to become pregnant. It is not known if ARISTADA will harm your unborn baby. If you become pregnant while taking ARISTADA, talk to your healthcare provider about registering with the National Pregnancy Registry for Atypical Antipsychotics. You can register by calling 1-866-961-2388, or visit http://womensmentalhealth.org/clinical-and-research-programs/pregnancyregistry/.
- are breastfeeding or plan to breastfeeding. ARISTADA can pass into your milk. It is not known if it may harm your baby. Talk to your healthcare provider about the best way to feed your baby if you receive ARISTADA.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. ARISTADA and other medicines may affect each other causing possible serious side effects. Do not start or stop any medicines while taking ARISTADA without talking to your healthcare provider first.

If you have any questions about your health or medicines, talk to your healthcare provider.

Please see U.S. FULL PRESCRIBING INFORMATION, including Boxed WARNING, and Medication Guide, for ARISTADA.

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2 Aristada [package insert], Waltham, MA; Alkermes, Inc.; 2015