

# Key Opinion Leader (KOL) Insights On a 2-Month Dosing Option



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Affecting an estimated 2.4 million American adults, schizophrenia is a serious and lifelong neurodevelopmental disorder that affects how a person thinks, feels, and behaves.<sup>1,2</sup> Symptoms associated with schizophrenia, including delusions, hallucinations, and disorganized thinking can be upsetting to patients with schizophrenia and those around them.<sup>2,3</sup>

Treatment with a long-acting injectable (LAI) provides several benefits. An LAI provides knowledge that a patient has received their therapy. Clinicians are aware if and when a patient misses an injection, which allows for prompt intervention, and the drug remains in the patient's system during extended dosing intervals, which may be important during transitions of care.<sup>4-6</sup>

ARISTADA® (aripiprazole lauroxil) is an LAI indicated for the treatment of schizophrenia in adults.<sup>7</sup> ARISTADA INITIO® (aripiprazole lauroxil), in combination with oral aripiprazole, is indicated for the initiation of ARISTADA when used for the treatment of schizophrenia in adults.<sup>8</sup> Both products carry a Boxed Warning that states “Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. ARISTADA and ARISTADA INITIO are not approved for the treatment of patients with dementia-related psychosis.”<sup>7,8</sup> ARISTADA offers the first and only 2-month dosing option (1064 mg) for schizophrenia, and the 2-month dosing option can be started at treatment initiation without prior treatment with a monthly LAI.<sup>7</sup> Both products are

only to be administered as an intramuscular injection by a healthcare professional. For patients who have never taken aripiprazole, establish tolerability with oral aripiprazole prior to initiating treatment with ARISTADA and ARISTADA INITIO.<sup>7,8</sup>

For all dosage strengths, ARISTADA can be started with one injection of ARISTADA INITIO and a single 30 mg dose of oral aripiprazole with the first injection of ARISTADA. If not starting ARISTADA with ARISTADA INITIO, administer 21 consecutive days of oral aripiprazole with the first ARISTADA injection.<sup>7,8</sup> ARISTADA INITIO is only available at a single strength as a single-dose pre-filled syringe, so dose adjustments are not possible.<sup>8</sup> Avoid use of ARISTADA INITIO in patients who are known CYP2D6 poor metabolizers or taking strong CYP3A4 inhibitors, strong CYP2D6 inhibitors, or strong CYP3A4 inducers, antihypertensive drugs or benzodiazepines.<sup>8</sup> The dose of ARISTADA may be adjusted as needed. When making dose and dosing interval adjustments, the pharmacokinetics and prolonged-release characteristics of ARISTADA should be considered.<sup>7</sup>

In this newsletter, three key opinion leaders—Henry Nasrallah, Leslie Citrome, and Rakesh Jain—share their experiences with LAIs, ARISTADA, and the potential benefits of a 2-month dosing option (1064 mg).

Learn more at [www.aristadahcp.com](http://www.aristadahcp.com)

## INDICATION

ARISTADA INITIO® (aripiprazole lauroxil), in combination with oral aripiprazole, is indicated for the initiation of ARISTADA when used for the treatment of schizophrenia in adults.

ARISTADA® (aripiprazole lauroxil) is indicated for the treatment of schizophrenia in adults.

## IMPORTANT SAFETY INFORMATION FOR ARISTADA INITIO AND ARISTADA

### **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. ARISTADA INITIO and ARISTADA are not approved for the treatment of patients with dementia-related psychosis.**

ARISTADA  
INITIO®  
aripiprazole lauroxil  
extended-release injectable suspension

675 mg

ARISTADA®  
aripiprazole lauroxil  
extended-release injectable suspension

441 mg 662 mg 882 mg 1064 mg

**Alkermes**

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning, for ARISTADA INITIO and ARISTADA.

“I have always been a strong advocate for long-acting injectable antipsychotic use in the pharmacotherapy of schizophrenia. Although LAIs are often regarded as a “last-resort” intervention, I have observed the clinical benefits of employing LAIs earlier in patients diagnosed with schizophrenia. LAIs ensure that the antipsychotic medication is being consistently delivered throughout the dosing interval.”



**Henry A. Nasrallah, MD**  
Emeritus Professor  
Psychiatry and Behavioral Neuroscience  
University of Cincinnati  
Cincinnati, OH

## Opportunities for a 2-Month (1064 mg) Dosing Option

An LAI formulation of an antipsychotic may also be considered when patients are transitioning between settings.<sup>9</sup>

There are a number of possible approaches to improve continuity of care for patients during transition periods, many of which revolve around communication (between clinicians and/or with patients) and engagement (from the patient, their family members, friends, and/or others).<sup>10-11</sup>

ARISTADA® continues to deliver consistent and sustained medication levels during the dosing interval, which is important during the transition from inpatient to outpatient care.<sup>7</sup> ARISTADA can be initiated prior to discharge, while other aspects of reentry into the community such as housing, insurance coverage, and sites for follow-up care are identified by the care team.<sup>12-14</sup>

ARISTADA INITIO® and ARISTADA® are available via the Hospital In-Patient Free Trial Program to initiate in this setting; see [www.aristadacaresupport.com](http://www.aristadacaresupport.com) for more information, including restrictions and eligibility requirements.



“Of utmost importance in creating the technology behind a 2-month dosing interval is demonstrating consistent and sustained medication levels during the dosing interval. Once tolerability is established, patients can start on the 2-month dose without first titrating from a previous monthly dosing schedule.”



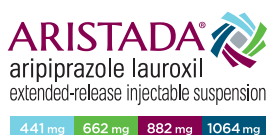
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Clinical Professor of Psychiatry  
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New York Medical College  
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### IMPORTANT SAFETY INFORMATION (continued)

**Contraindication:** Known hypersensitivity reaction to aripiprazole. Reactions ranged from pruritus/urticaria to anaphylaxis.

**Cerebrovascular Adverse Reactions, Including Stroke:** Increased incidence of cerebrovascular adverse reactions (eg, stroke, transient ischemic attack), including fatalities, have been reported in placebo-controlled trials of elderly patients with dementia-related psychosis treated with risperidone, aripiprazole, and olanzapine. ARISTADA INITIO and ARISTADA are not approved for the treatment of patients with dementia-related psychosis.

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“To be able to extend patients’ dosing interval to 2 months is a really big deal. In my opinion, the 2-month dosing option of 1064 mg does not decrease the frequency that I see my patients. We still like to keep monthly appointments, but now instead of each being solely focused on medication management we talk about other important aspects of the patient’s life that are equally relevant.”



**Rakesh Jain, MD, MPH**

Clinical Professor  
Department of Psychiatry  
Texas Tech Health Sciences Center School of Medicine  
Midland, Texas

## When patients have transitioned to outpatient care, the 1064 mg dose may continue to be administered every 2 months in addition to regular follow-up visits<sup>7</sup>



### Outpatient Setting

With LAI antipsychotic medications, there is greater assurance that a patient will receive medication continuously because there are fewer opportunities to miss a medication dose and clinicians will be immediately aware of a missed visit or injection.<sup>9</sup> According to a retrospective study of 71,776 subjects published in 2017, approximately 40% of Schizophrenia patients did not receive outpatient follow-up care within 30 days of discharge.<sup>15</sup> Disengagement from care is a well-known challenge in the treatment of schizophrenia.<sup>16</sup>

Your adult patients with schizophrenia may have the option of 6 injections per year (with the 1064 mg dosing option), and regularly scheduled visits can continue to address your patients’ needs.<sup>7</sup>

Product samples are available. Contact your representative now to order samples for your practice at <https://www.aristadahcp.com/product-samples>.

## IMPORTANT SAFETY INFORMATION (continued)

**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 in contrast to ARISTADA which is administered monthly, every 6 weeks, or every 8 weeks. Do not substitute ARISTADA INITIO for ARISTADA because of differing pharmacokinetic profiles.

**Tardive Dyskinesia (TD):** The risk of developing TD (a syndrome of abnormal, involuntary movements) and the potential for it to become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic increase. The syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. Prescribing antipsychotics should be consistent with the need to minimize TD. Discontinue ARISTADA if clinically appropriate. TD may remit, partially or completely, if antipsychotic treatment is withdrawn.

Please see additional Important Safety Information throughout and accompanying full Prescribing Information, including Boxed Warning, for ARISTADA INITIO and ARISTADA.

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aripiprazole lauroxil  
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1. National Alliance on Mental Illness. Mental Health Facts in America. Accessed February 25, 2021. <https://www.nami.org/nami/media/nami-media/infographics/generalmhfacts.pdf>. 2. National Institute of Mental Health. Schizophrenia. NIH Publication No. 19-MH-8082. 3. Kay SR, Fiszbein A, Opler LA. The Positive and Negative Syndrome Scale (PANSS) for schizophrenia. *Schizophr Bull.* 1987;13:261-276. 4. Brissos S, Veguilla MR, Taylor D, Balanzá-Martínez V. The role of long-acting injectable antipsychotics in schizophrenia: a critical appraisal. *Ther Adv Psychopharmacol.* 2014;4:198-219. 5. Kane JM. Strategies for improving compliance in treatment of schizophrenia by using a long-acting formulation of an antipsychotic: Clinical Studies. *J Clin Psychiatry.* 2003;64(suppl 16):34-40. 6. Correll CU, Haddad PM, Lauriello J, et al. The use of long-acting injectable antipsychotics in schizophrenia: evaluating the evidence. *J Clin Psychiatry.* 2016;77(suppl 3):1-24. 7. ARISTADA [prescribing information]. Waltham, MA: Alkermes, Inc; 2021. 8. ARISTADA INITIO [prescribing information]. Waltham, MA: Alkermes, Inc; 2021. 9. *APA Practice Guideline for the Treatment of Patients With Schizophrenia.* 3rd ed. American Psychiatric Association; 2021. 10. Olfson M, Mechanic D, Boyer CA, Hansell S. Linking inpatients with schizophrenia to outpatient care. *Psychiatr Serv.* 1998;49:911-917. 11. Boyer CA, McAlpine DD, Pottick KJ, Olfson M. Identifying Risk factors and key strategies in linkage to outpatient psychiatric care. *Am J Psychiatry.* 2000;157:1592-1598. 12. Farley JF, Wang C, Hansen RA, et al. Continuity of antipsychotic medication management for Medicaid patients with schizophrenia. *Psychiatr Serv.* 2011;62:747-752. 13. Fortney J, Sullivan G, Williams K, et al. Measuring continuity of care for clients of public mental health systems. *Health Serv Res.* 2003;38:1157-1175. 14. Velligan Factors Influencing Adherence to Treatment Plans. In: *Schizophrenia and Psychotic Spectrum Disorders.* Eds, Schulz SC, Green MF, Nelson KJ. Oxford University Press. 2016. 15. Marcus Chuang CC, Ng-Mak DS, Olfson M. Outpatient follow-up care and risk of hospital readmission in schizophrenia and bipolar disorder. *Psychiatric Services* 2017;68(12):1239-1246. 16. O'Brien A, Fahmy R, Singh SP. Disengagement from mental health services. *Soc Psychiatry Psychiatr Epidemiol.* 2009;44:558-568.

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

**INDICATION**

ARISTADA INITIO, in combination with oral aripiprazole, is indicated for the initiation of ARISTADA when used for the treatment of schizophrenia in adults. ARISTADA is indicated for the treatment of schizophrenia in adults.

**IMPORTANT SAFETY INFORMATION**

**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. ARISTADA INITIO and ARISTADA are not approved for the treatment of patients with dementia-related psychosis.

**Contraindication:** Known hypersensitivity reaction to aripiprazole. Reactions have ranged from pruritus/urticaria to anaphylaxis.

**Cerebrovascular Adverse Reactions, Including Stroke:**

Increased incidence of cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack), including fatalities, have been reported in placebo-controlled trials of elderly patients with dementia-related psychosis treated with risperidone, aripiprazole, and olanzapine. ARISTADA INITIO and ARISTADA are 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 in contrast to ARISTADA which is administered monthly, every 6 weeks, or every 8 weeks. Do not substitute ARISTADA INITIO for ARISTADA because of differing pharmacokinetic profiles.

**Neuroleptic Malignant Syndrome (NMS):**

A potentially fatal symptom complex may occur with administration of antipsychotic drugs, including ARISTADA INITIO and ARISTADA. Clinical manifestations of NMS include 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):** The risk of developing TD (a syndrome of abnormal, involuntary movements) and the potential for it to become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic increase. The syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. Prescribing antipsychotics should be consistent with the need to minimize TD. Discontinue ARISTADA if clinically appropriate. TD may remit, partially or completely, if antipsychotic treatment is withdrawn.

**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 antipsychotic use. 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 sexual urges, shopping, binge 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 and risk of dehydration and syncope.

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

**Leukopenia, Neutropenia, and Agranulocytosis:**

Leukopenia, neutropenia and agranulocytosis have been reported with antipsychotics. Monitor complete blood count in patients with pre-existing low white blood cell count (WBC)/absolute neutrophil count or history of drug-induced leukopenia/neutropenia. Discontinue ARISTADA INITIO and/or ARISTADA at the first sign of a clinically significant decline in WBC and in severely neutropenic patients.

**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 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. Advise patients regarding appropriate care in avoiding overheating and dehydration. Appropriate care is advised for patients who may exercise 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 may be recommended if patients are 1) known as CYP2D6 poor metabolizers and/or 2) taking strong CYP3A4 inhibitors, strong CYP2D6 inhibitors, or strong 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 monthly) 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%, 5%, 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.

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