CLINICAL STUDIES

SUPPORT THE EFFICACY AND SAFETY OF ARISTADA®
(aripiprazole lauroxil)

Pivotal trial

52-week safety study

ALPINE active-controlled study

INDICATION

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

ARISTADA 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.

Please see additional Important Safety Information on pages 12 to 13 and accompanying full Prescribing Information, including Boxed Warning, for ARISTADA INITIO and ARISTADA.

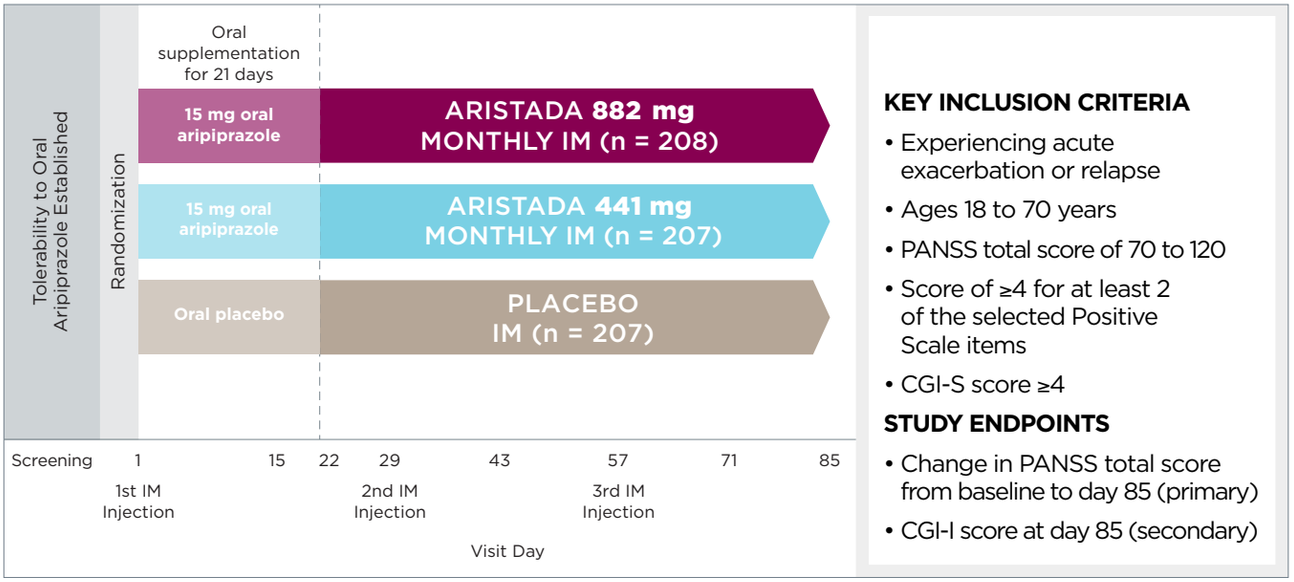
ARISTADA INITIO®
aripiprazole lauroxil
extended-release injectable suspension
675 mg

+

ARISTADA®
aripiprazole lauroxil
extended-release injectable suspension
441 mg | 662 mg | 882 mg | 1064 mg

Pivotal trial: A 12-week, phase 3, randomized, double-blind, placebo-controlled, fixed-dose study evaluating the efficacy and safety of ARISTADA in adults with schizophrenia[1,2]

ARISTADA PIVOTAL TRIAL DESIGN (N = 622)[1,2]



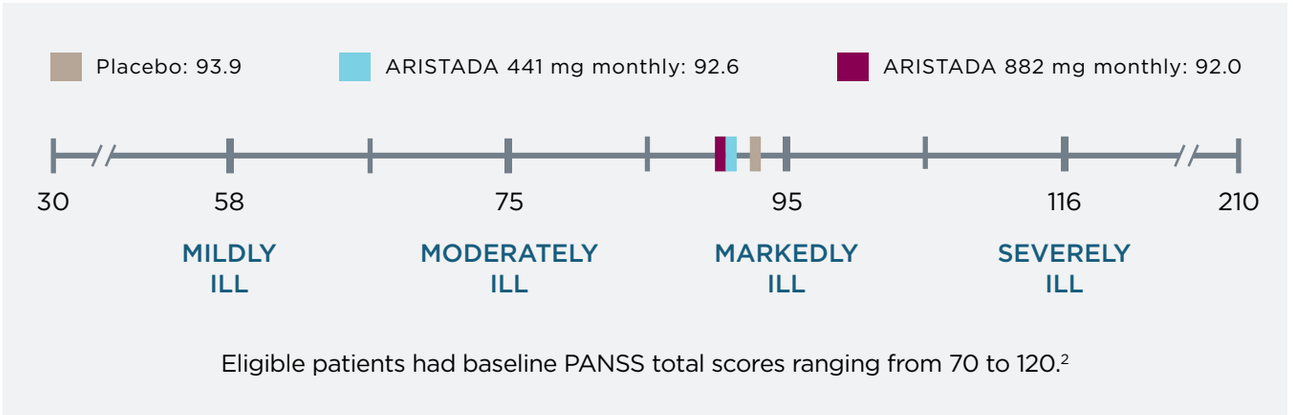
Abbreviations: CGI-I, Clinical Global Impression-Improvement; CGI-S, Clinical Global Impression-Severity of Illness; IM, intramuscular; PANSS, Positive and Negative Syndrome Scale.

Vertical dotted line indicates end of oral supplementation.

ARISTADA was shown to reduce PANSS total scores in markedly ill patients[1,3]

Patients enrolled in the 12-week clinical trial were considered markedly ill, with mean baseline PANSS total scores of 93.9 (placebo), 92.6 (ARISTADA® [aripiprazole lauroxil] 441 mg monthly), and 92.0 (ARISTADA 882 mg monthly).[1,3]

MEAN BASELINE PANSS TOTAL SCORES[1]



Eligible patients had baseline PANSS total scores ranging from 70 to 120.[2]

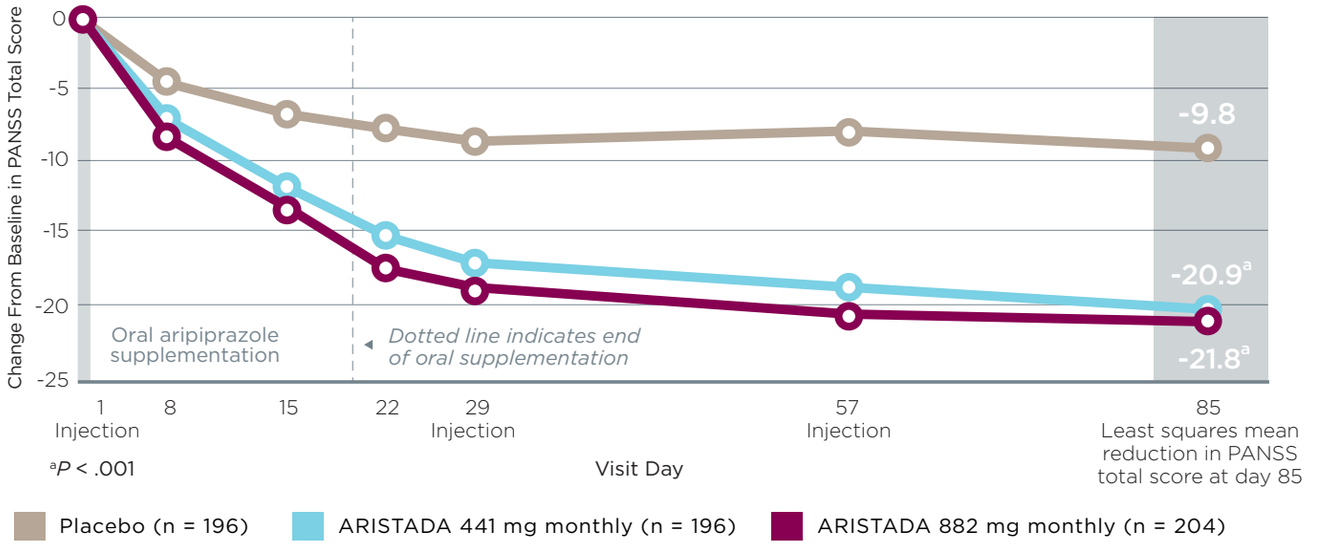
IMPORTANT SAFETY INFORMATION FOR ARISTADA INITIO AND ARISTADA

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 (continued)

In a phase 3 study, ARISTADA was shown to reduce schizophrenia symptoms[1,2]

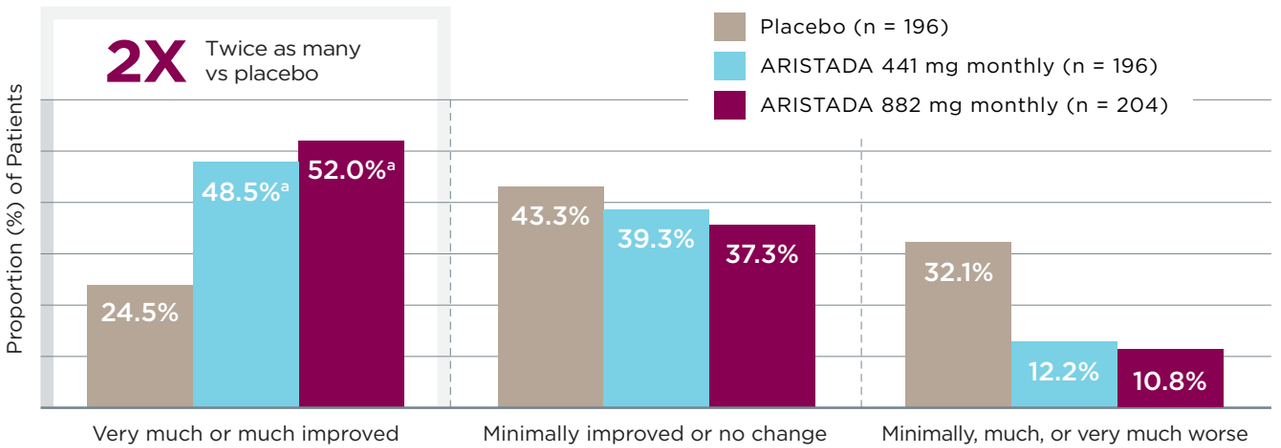
2X GREATER MEAN REDUCTION IN PANSS TOTAL SCORE VS PLACEBO AT DAY 85 (PRIMARY ENDPOINT)[1,2]



ARISTADA patients experienced an improvement in clinical condition[2,4]

- The CGI-I scale allows the clinician to assess and rate improvement in schizophrenia on a scale of 1 (very much improved) to 7 (very much worse) based on the change in clinical condition from baseline[1]

CGI-I SCORE AT DAY 85 (SECONDARY ENDPOINT)[2,4]



aP < .001

- 2 times as many patients receiving ARISTADA® (aripiprazole lauroxil) had CGI-I scores that were very much improved or much improved at day 85 vs placebo (secondary endpoint)[4]

IMPORTANT SAFETY INFORMATION FOR ARISTADA INITIO AND ARISTADA

Cerebrovascular Adverse Reactions, Including Stroke (continued): 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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ARISTADA has been evaluated for safety in 1180 adult patients in clinical trials in schizophrenia[1]

ADVERSE REACTIONS IN ≥2% OF ARISTADA-TREATED PATIENTS AND THAT OCCURRED AT GREATER INCIDENCE THAN IN PLACEBO-TREATED PATIENTS IN THE 12-WEEK CLINICAL TRIAL[1]

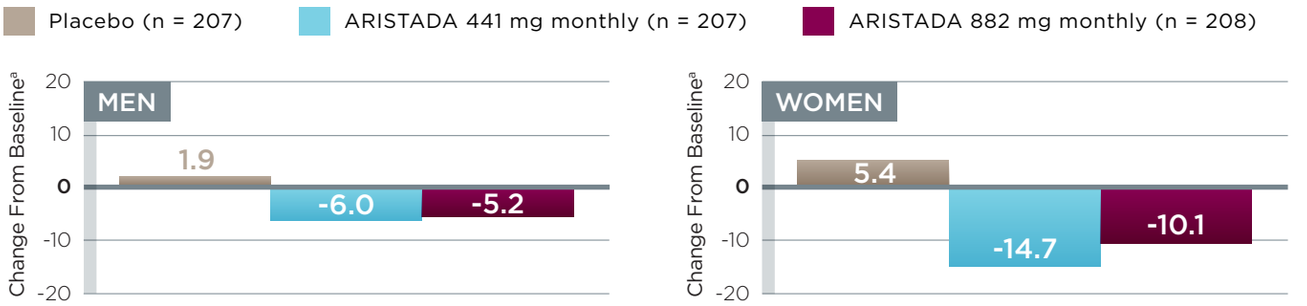
Adverse reactions	Placebo (n = 207)	ARISTADA 441 mg monthly (n = 207)	ARISTADA 882 mg monthly (n = 208)
Injection-site pain	2%	3%	4%
Increased weight	1%	2%	2%
Increased blood creatine phosphokinase	0%	2%	1%
Akathisia	4%	11%	11%
Headache	3%	3%	5%
Insomnia	2%	3%	4%
Restlessness	1%	3%	1%

- In an open-label pharmacokinetic study, adverse reactions associated with the use of ARISTADA® (aripiprazole lauroxil) were similar across the 441 mg monthly, 882 mg every 6 weeks, and 1064 mg every 2 months dose groups[1]

DISCONTINUATIONS

- In the 12-week clinical trial, discontinuations due to adverse events in patients receiving ARISTADA were lower than for placebo: 6.8% for the 441 mg dose, 2.9% for the 882 mg dose, and 17.9% for placebo[2]
- In the placebo group, adverse events leading to discontinuation were related to exacerbation of psychosis/schizophrenia. Otherwise, adverse events leading to discontinuation were similar between the 3 treatment groups[4]

PROLACTIN LEVELS AT BASELINE AND LAST POST-BASELINE VISIT[5]



[a]Mean baseline prolactin: placebo: 10.1 (men), 28.8 (women); ARISTADA 441 mg monthly: 10.3 (men), 27.1 (women); ARISTADA 882 mg monthly: 10.2 (men), 25.7 (women). Normal prolactin: 4.0 to 15.2 ng/mL (men), 4.8 to 23.3 ng/mL (women).[5]

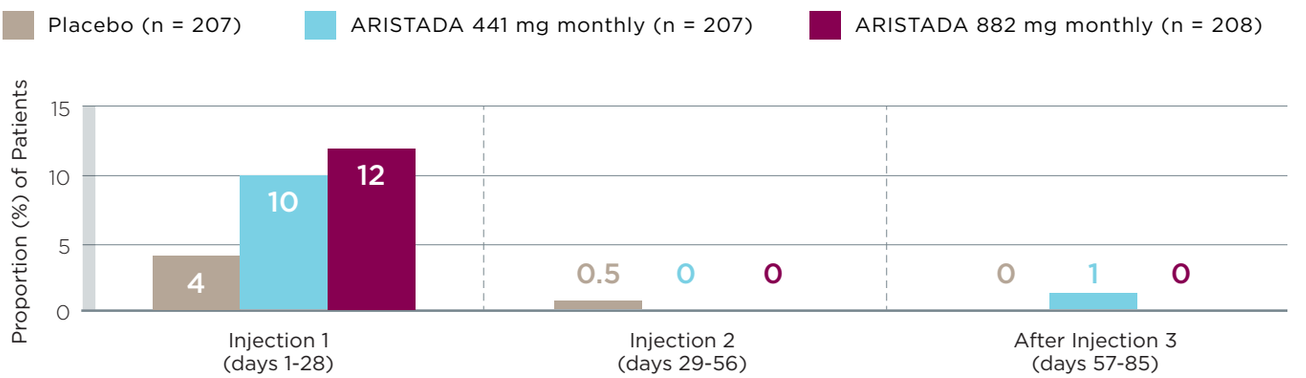
- In the 12-week clinical trial, mean prolactin levels decreased below baseline measurements starting at day 29 through day 85 in both ARISTADA groups compared with placebo[5]
- Baseline prolactin levels may have been affected by previous antipsychotic medication use prior to starting the study[4]
- Patients in the clinical trial had previously established tolerability to aripiprazole, which may affect prolactin measurements[2]

MEAN INCREASE IN BODY WEIGHT FROM BASELINE TO LAST POST-BASELINE ASSESSMENT[5]

PLACEBO (N = 207)	ARISTADA 441 mg (N = 207)	ARISTADA 882 mg (N = 208)
0.02 lb	1.6 lb	1.9 lb

- In the 12-week clinical trial, mean increase in body weight from baseline to last post-baseline assessment was 0.02 pounds for placebo (n = 207), 1.6 pounds for ARISTADA 441 mg monthly (n = 207), and 1.9 pounds for ARISTADA 882 mg monthly (n = 208)[5]
- The percentage of patients with ≥7% increase in weight noted at the last post-baseline visit during the treatment period was 6% for placebo, 10% for ARISTADA 441 mg monthly, and 9% for ARISTADA 882 mg monthly[1]

AKATHISIA ONSET RELATIVE TO INJECTION NUMBER AND STUDY DAY[4]



- Akathisia was the most common adverse reaction (incidence ≥5% and at least twice the rate of placebo in patients treated with ARISTADA in the 12-week clinical trial)[1]
- 2 out of 415 patients discontinued ARISTADA due to akathisia, which was not dose-related[4]
- Benzodiazepines and short-acting beta-blockers were permitted for treatment-emergent akathisia as needed[4]

INJECTION-SITE PAIN

- In the phase 3 clinical trial, overall injection-site reactions were reported in 2% (placebo), 4% (441 mg monthly), and 5% (882 mg monthly) of patients[1]
  - Of these, the incidence of pain with the first injection was 2%, 3%, and 4%, respectively, and ≤1% with each subsequent injection. Other injection-site reactions (induration, swelling, and redness) were <1%[1]

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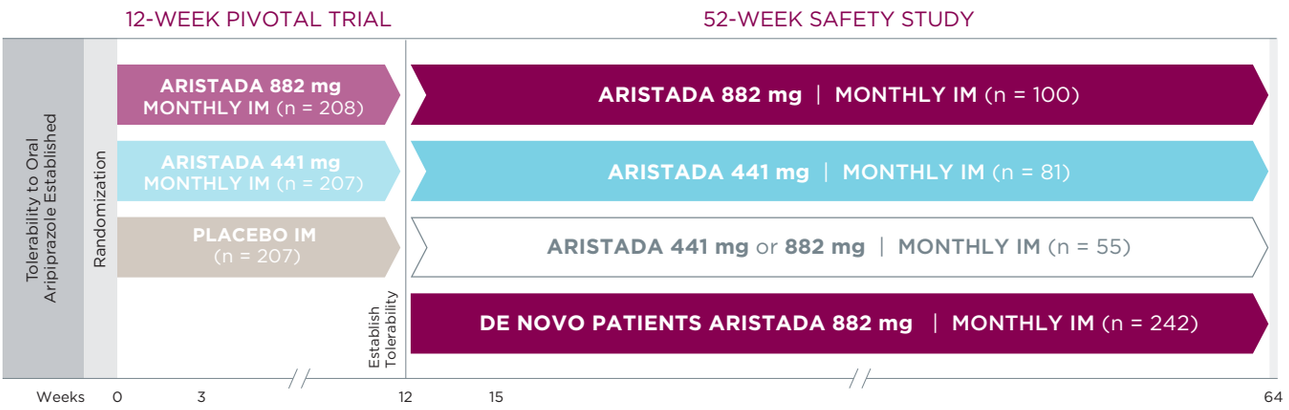
52-week safety study: Assessing the long-term safety and tolerability of ARISTADA in patients with stable schizophrenia[6]

52-WEEK OPEN-LABEL SAFETY STUDY DESIGN[6]



- The primary objective was to assess the long-term safety and tolerability of ARISTADA® (aripiprazole lauroxil) in patients with stable schizophrenia[6]
- The study enrolled 236 patients who completed the 12-week phase 3 study, as well as 242 new adults with chronic stable schizophrenia, all of who were administered 882 mg of ARISTADA by intramuscular injection every 4 weeks[6]
- Patients on prior placebo and de novo patients received active oral aripiprazole 21-day supplementation, whereas patients who had received prior active ARISTADA received placebo[6]

ADVERSE EVENTS OCCURRING IN ≥2% OF PATIENTS DURING THE 52-WEEK STUDY[6]

AE	ARISTADA 441 mg monthly (N = 110)	ARISTADA 882 mg monthly (N = 368)	Both ARISTADA doses (N = 478)
Any AE	46%	52%	50%
Insomnia	3%	10%	8%
Weight increased	6%	5%	5%
Anxiety	4%	5%	4%
Injection-site pain	1%	5%[a]	4%
Akathisia	1%	5%	4%
Headache	6%	3%	4%
Schizophrenia	4%	3%	3%
Nasopharyngitis	4%	3%	3%
Weight decreased	3%	2%	3%
Tremor	1%	3%	3%

Abbreviation: AE, adverse event.
[a]Majority reported in de novo patients (16 patients).

- Adverse events leading to discontinuation were reported in 5.9% (n = 28) of the total population (N = 478)[6]
- Adverse events were generally consistent with what is established and known of the safety of aripiprazole[6]
- No new safety events were observed during this 52-week safety study[6]

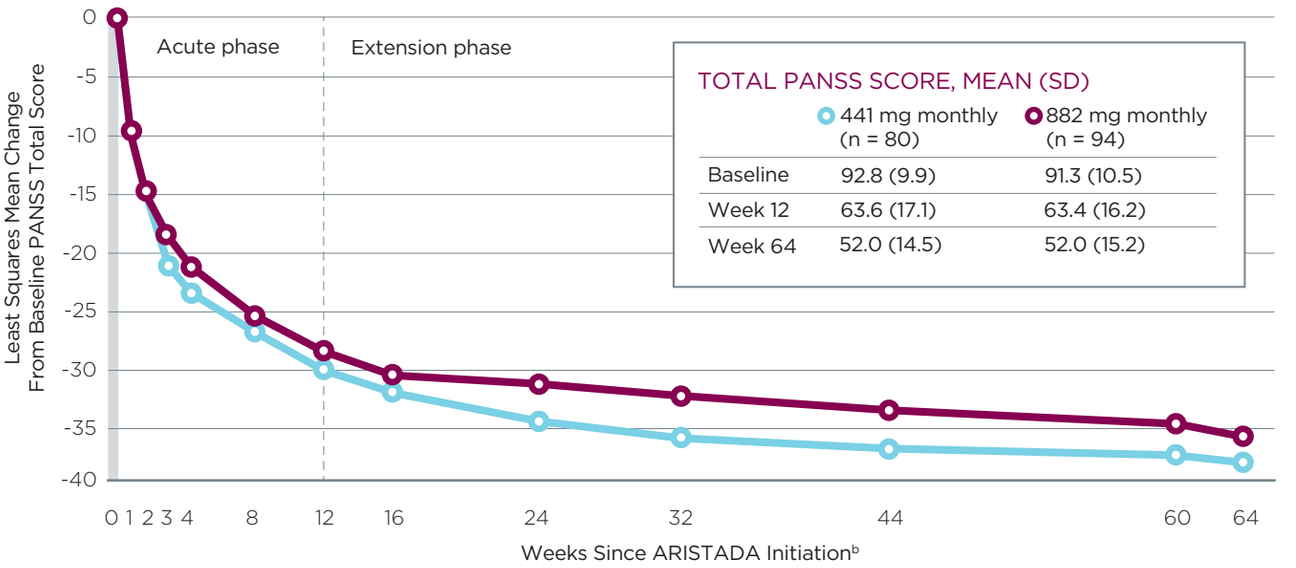
The durability of effect of ARISTADA was observed over the 52-week safety study period (secondary outcome)[6]

- The results of the study demonstrate the safety and tolerability of long-term treatment with aripiprazole lauroxil in patients with schizophrenia

Long-term efficacy was further evaluated in a post hoc analysis[7]

- A post hoc analysis assessed long-term outcomes for a subgroup of patients (N = 174) who entered a 52-week safety study after being successfully stabilized during a pivotal 12-week, placebo-controlled, randomized clinical trial and had at least 1 PANSS assessment after drug administration in the safety study*
- Patients received 1 of 2 doses of ARISTADA (441 mg or 882 mg) administered by intramuscular injection every 4 weeks during both the 12-week study and the 52-week safety study
- The objective was to evaluate the durability of the therapeutic effect of long-term treatment with ARISTADA in patients with schizophrenia following successful treatment of an acute psychotic episode
- Patients from the acute-phase study who continued in the 52-week study were observed to have sustained and gradual improvements in PANSS total score for both dose groups through week 64 (least squares mean [standard error] change from week 12 was -8.1 [1.3] and -7.2 [1.2] for the 441 mg and 882 mg cohorts, respectively)*

MEAN CHANGE FROM BASELINE IN PANSS TOTAL SCORE IN THE ACTIVE ROLLOVER PATIENT SUBGROUP[7,a]



TOTAL PANSS SCORE, MEAN (SD)

	441 mg monthly (n = 80)	882 mg monthly (n = 94)
Baseline	92.8 (9.9)	91.3 (10.5)
Week 12	63.6 (17.1)	63.4 (16.2)
Week 64	52.0 (14.5)	52.0 (15.2)

Abbreviation: SD, standard deviation.
[a]In patients who had at least 1 PANSS assessment after drug administration in the 52-week safety study.[7]
[b]Indicated weeks denote assessment time points.[7]

*This post hoc analysis of active rollover patients from the 12-week acute-phase study was not designed to prospectively assess, nor was it powered to examine, the efficacy of ARISTADA in the subgroup of patients. No definitive conclusions of the efficacy can be drawn from these results.

In addition to the inherent limitations of post hoc analyses, limitations of this analysis include the preferential selection of study participants and differing assessment intervals between the 12-week study and the 52-week safety study.[7]

IMPORTANT SAFETY INFORMATION FOR ARISTADA INITIO AND ARISTADA

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.

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ALPINE*: A phase 3b, multicenter, randomized, double-blind, active-controlled study evaluating the efficacy and safety of ARISTADA INITIO® (aripiprazole lauroxil) and the ARISTADA® (aripiprazole lauroxil) 2-month dose (1064 mg) or INVEGA SUSTENNA® (paliperidone palmitate) monthly[4]

- The primary objective was to evaluate the efficacy of ARISTADA INITIO† plus 30 mg of oral aripiprazole (ARISTADA INITIO regimen) and ARISTADA 1064 mg during the first 4 weeks of treatment in adult patients hospitalized for an acute exacerbation of schizophrenia[4]

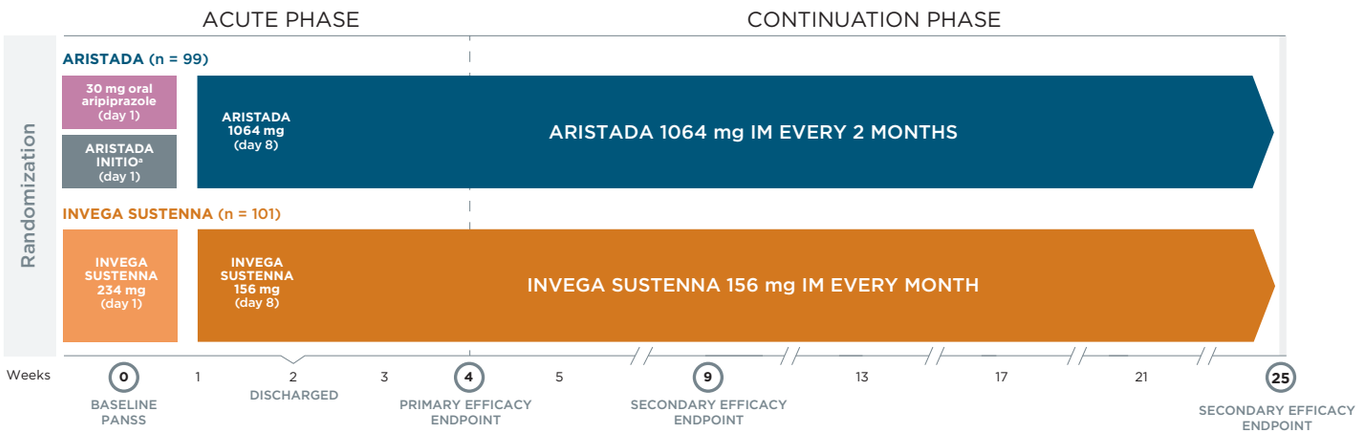
PRIMARY EFFICACY ENDPOINT[4]

- Change in PANSS total score from baseline to Week 4 (within group)‡

SECONDARY EFFICACY ENDPOINTS[4]

- Change in PANSS total score from baseline to Week 9 and Week 25 (within group)‡
- Change in PANSS total score at Weeks 4, 9, and 25 between the 2 treatment groups (between group)§

ALPINE PHASE 3B STUDY DESIGN[4]



Placebo intramuscular (IM) injections and an oral placebo were given to maintain blinding.

[a]ARISTADA INITIO is a onetime initiation IM injection.

- INVEGA SUSTENNA, a known and effective treatment, served as an active control. An active drug with a known efficacy profile is a useful method for evaluating new drugs while avoiding the ethical dilemmas associated with placebo[4]
- The study was not designed to compare efficacy or safety between groups[4]
- Patients were hospitalized with an acute exacerbation of schizophrenia and considered markedly ill, with mean PANSS total scores at baseline of 94.1 (ARISTADA) and 94.6 (INVEGA SUSTENNA)[3,4]
- Prior to the study, 31% of the subjects had a history of exposure to risperidone/paliperidone only, 6% of the subjects had a history of exposure to aripiprazole only, 50% of the subjects had a history of exposure to both, and 13% of the subjects had no exposure to either of the antipsychotics[4]
- Patients had to have a history of tolerated use of aripiprazole or risperidone/paliperidone, or demonstrated tolerability to perspective oral test doses during study screening[4]

**Abbreviation: ALPINE, Aripiprazole Lauroxil and Paliperidone palmitate: INitiation Effectiveness.*
†ARISTADA INITIO was approved by the FDA through a single pharmacokinetic bridging study.
‡Within group: the separate assessment of each treatment group in the change from baseline in PANSS total score at Weeks 4, 9, and 25.
§Between group: the assessment of the difference in PANSS total score between treatment groups at Weeks 4, 9, and 25.

IMPORTANT SAFETY INFORMATION FOR ARISTADA INITIO AND ARISTADA

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; (continued)

Reduction in PANSS total score from baseline was observed for the treatment group receiving ARISTADA INITIO and the ARISTADA 2-month dose (1064 mg)[4]

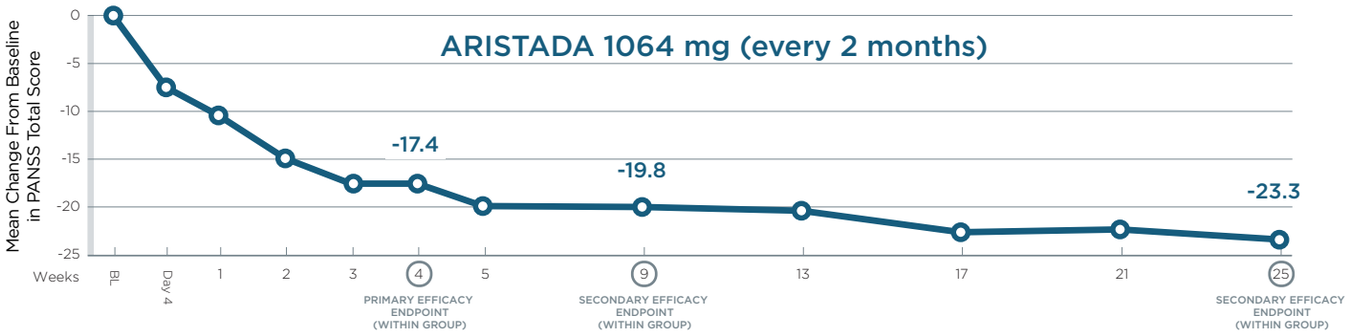
PRIMARY ENDPOINT[4]

- There was improvement from baseline to Week 4 for each treatment group
- Mean change from baseline in PANSS total score was -17.4 for ARISTADA

SECONDARY ENDPOINTS[4]

- Within-group reductions in change from baseline in PANSS total scores were observed during the 25-week study for each treatment group

MEAN CHANGE FROM BASELINE IN PANSS TOTAL SCORE (WITHIN GROUP)[4]



This was not a head-to-head study. This study was not powered to provide comparative efficacy or safety results and should not be interpreted as suggesting ARISTADA as superior or noninferior to INVEGA SUSTENNA.[4]

EVALUATION OF PATIENT CONTINUATION AND SAFETY/TOLERABILITY[4]

PATIENT DISPOSITION[4]	**ARISTADA** (N = 99) n (%)
Completed the 4-week treatment period[a]	79 (80%)
Completed the entire treatment period	56 (57%)

ADVERSE EVENTS REPORTED OVER THE FULL 25 WEEKS[4]	**ARISTADA** (N = 99) n (%)
Any AE[b]	69 (70%)
Serious AEs	8 (8%)
AEs ≥5%[c]	
Injection-site pain	17 (17%)
Weight increased	9 (9%)
Akathisia	9 (9%)
Headache	8 (8%)
Schizophrenia	5 (5%)
Somnolence	4 (4%)
Dystonia	3 (3%)
AE leading to treatment discontinuation	10 (10%)

- Additional laboratory values were measured[4]

[a]Patients with a week 4 PANSS assessment.
[b]All AEs reported during treatment while in the study.
[c]Shown in descending order of incidence.

IMPORTANT SAFETY INFORMATION FOR ARISTADA INITIO AND ARISTADA

Neuroleptic Malignant Syndrome (NMS) (continued): 2) intensive symptomatic treatment and medical monitoring; and 3) treatment of any concomitant serious medical problems for which specific treatments are available.

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Reduction in PANSS total score from baseline was observed for the treatment group receiving INVEGA SUSTENNA 156 mg every month[4]

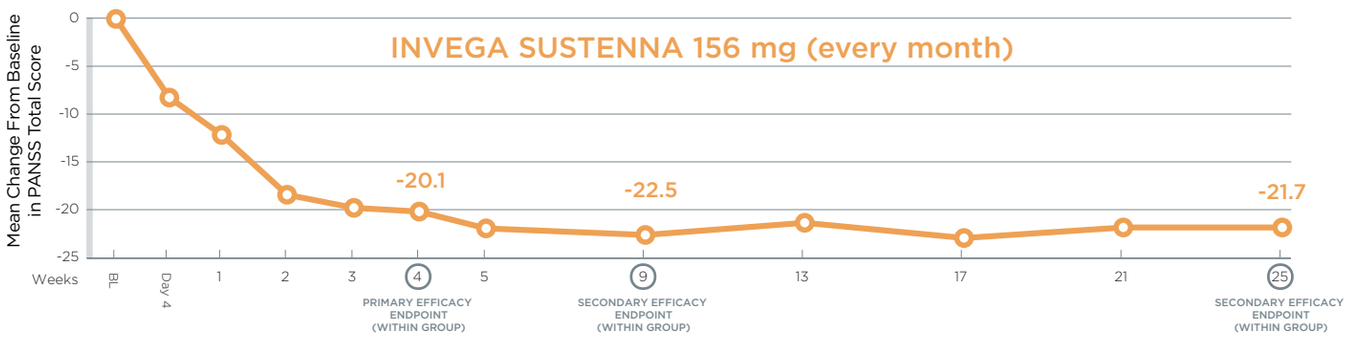
PRIMARY ENDPOINT[4]

- There was improvement from baseline to Week 4 for each treatment group
- Mean change from baseline in PANSS total score was -20.1 for INVEGA SUSTENNA® (paliperidone palmitate)

SECONDARY ENDPOINTS[4]

- Within-group reductions in change from baseline in PANSS total scores were observed during the 25-week study for each treatment group

MEAN CHANGE FROM BASELINE IN PANSS TOTAL SCORE (WITHIN GROUP)[4]



This was not a head-to-head study. This study was not powered to provide comparative efficacy or safety results and should not be interpreted as suggesting ARISTADA as superior or noninferior to INVEGA SUSTENNA.[4]

EVALUATION OF PATIENT CONTINUATION AND SAFETY/TOLERABILITY[4]

PATIENT DISPOSITION[4]	**INVEGA SUSTENNA** (N = 101) n (%)
Completed the 4-week treatment period[a]	75 (74%)
Completed the entire treatment period	43 (43%)

ADVERSE EVENTS REPORTED OVER THE FULL 25 WEEKS[4]	**INVEGA SUSTENNA** (N = 101) n (%)
Any AE[b]	72 (71%)
Serious AEs	7 (7%)
AEs ≥5%[c]	
Injection-site pain	25 (25%)
Weight increased	17 (17%)
Akathisia	11 (11%)
Headache	8 (8%)
Somnolence	7 (7%)
Dystonia	6 (6%)
Schizophrenia	2 (2%)
AE leading to treatment discontinuation	11 (11%)

- Additional laboratory values were measured[4]

[a]Patients with a week 4 PANSS assessment.
[b]All AEs reported during treatment while in the study.
[c]Shown in descending order of incidence.

IMPORTANT SAFETY INFORMATION FOR ARISTADA INITIO AND ARISTADA

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.

Hear more about the efficacy, safety, and pharmacokinetics of ARISTADA INITIO and ARISTADA

Visit ***aristadahcp.com/expert-insights***

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IMPORTANT SAFETY INFORMATION FOR ARISTADA INITIO AND ARISTADA

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.

IMPORTANT SAFETY INFORMATION FOR ARISTADA INITIO AND ARISTADA *(continued)*

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.

Please see accompanying full Prescribing Information, including Boxed Warning, for ARISTADA INITIO and ARISTADA.

References: 1. ARISTADA [package insert]. Waltham, MA: Alkermes, Inc; 2019. **2.** Meltzer HY, Risinger R, Nasrallah HA, et al. A randomized, double-blind, placebo-controlled trial of aripiprazole lauroxil in acute exacerbation of schizophrenia. *J Clin Psychiatry.* 2015;76(8):1085-1090. **3.** Leucht S, Kane JM, Kissling W, Hamann J, Etschel E, Engel RR. What does the PANSS mean? *Schizophr Res.* 2005;79(2-3):231-238. **4.** Data on file. Alkermes, Inc. **5.** Nasrallah HA, Newcomer JW, Risinger R, et al. Effect of aripiprazole lauroxil on metabolic and endocrine profiles and related safety considerations among patients with acute schizophrenia. *J Clin Psychiatry*. 2016;77(11):1519-1525. **6.** Nasrallah HA, Aquila R, Du Y, Stanford AD, Claxton A, Weiden PJ. Long-term safety and tolerability of aripiprazole lauroxil in patients with schizophrenia. *CNS Spectr.* 2018:1-9. **7.** McEvoy JP, Risinger R, Mykhnyak S, et al. Durability of therapeutic response with long-term aripiprazole lauroxil treatment following successful resolution of an acute episode of schizophrenia. *J Clin Psychiatry*. 2017;78(8):1103-1109. **8.** ARISTADA INITIO [package insert]. Waltham, MA: Alkermes, Inc; 2019.

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

FULLY DOSE ON DAY 1 FOR 2 MONTHS[1,8]

ARISTADA IS PROVEN EFFECTIVE FOR SCHIZOPHRENIA IN ADULTS

- It was shown to reduce symptoms of schizophrenia in a phase 3 study[1]
- The 52-week study showed safety and durability of therapeutic effect[6]
- Reduction in PANSS total score from baseline was observed for ARISTADA INITIO® (aripiprazole lauroxil) and the ARISTADA® (aripiprazole lauroxil) 2-month dose (1064 mg) at Week 4 in a post-marketing study[4]
- For patients who have never taken aripiprazole, establish tolerability with oral aripiprazole prior to initiating ARISTADA or ARISTADA INITIO[1,8]

*Go to **aristadahcp.com** to learn more.*

INDICATION

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

ARISTADA 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.

Please see additional Important Safety Information on pages 12 to 13 and accompanying full Prescribing Information, including Boxed Warning, for ARISTADA INITIO and ARISTADA.

Alkermes®

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