

**New Formulation - Aripiprazole Lauroxil NanoCrystal Dispersion Technology (Aristada Initio®)  
FDA Approved July 2018**

**Indication:** Aristada Initio is indicated for the initiation of Aristada® in combination with oral aripiprazole for the treatment of schizophrenia in adults

**Mechanism:** Aripiprazole lauroxil is a prodrug of aripiprazole. Aripiprazole functions as a partial agonist for serotonin 5-HT<sub>1A</sub> and dopamine D<sub>2</sub> receptors and as an antagonist at serotonin 5-HT<sub>2A</sub> receptors

**Dosage**

- Establish tolerability with oral aripiprazole before starting Aristada\*\*
- Administer 675 mg Aristada Initio and one 30 mg dose of oral aripiprazole in conjunction with the first Aristada injection
  - the 1<sup>st</sup> Aristada injection may be administered either on the same day or up to 10 days after Aristada Initio is given
- Aristada Initio is to be used as a single dose only to either initiate treatment with Aristada or to re-initiate treatment following a missed dose
- Aristada Initio and Aristada are not interchangeable due to differing PK profiles
- No dosage adjustment necessary in renal or hepatic impairment

**Administration**

- Administer Aristada Initio IM in either deltoid or gluteal muscle
- Tap the syringe at least 10 times and then shake vigorously ≥30 seconds to ensure uniform suspension
- If the syringe is not used within 15 minutes, shake again for 30 seconds
- Use the appropriate sized needle for the injection site. Inject in a rapid and continuous manner
- Avoid injecting both Aristada Initio and Aristada concomitantly into the same deltoid or gluteal muscle



**DDI**

- Avoid concomitant use of Aristada Initio with antihypertensives and benzodiazepines since Aristada Initio's dose cannot be adjusted
  - Aripiprazole has the potential to enhance the effect of certain antihypertensive agents (carvedilol, lisinopril, prazosin)
  - Aripiprazole may worsen sedation and orthostatic hypotension if used concomitantly with benzodiazepines (lorazepam)
- Avoid use in known CYP2D6 poor metabolizers
- Avoid use with strong CYP2D6 or CYP 3A4 inhibitors and strong CYP3A4 inducers

**Pharmacokinetics**

\*\*may take up to 2 weeks to fully assess tolerability based on oral aripiprazole half life

1. With the addition of the single Aristada Initio and a 30-mg oral aripiprazole with the 1<sup>st</sup> Aristada dose

- Aristada Initio uses NanoCrystal delivery system which provides an ER formulation using smaller nanometer-sized medication crystals of aripiprazole lauroxil compared to Aristada. The smaller particle size increases the rate of dissolution resulting in more rapid achievement of relevant aripiprazole level
- A single dose of Aristada Initio is sufficient for all dose levels of oral aripiprazole and aripiprazole lauroxil

<b>Onset</b>	reaches systemic circulation on day of injection; aripiprazole concentrations reach “relevant levels” within 4 days <sup>1</sup>
<b>Half-life elimination</b>	15–18 days
<b>Metabolism</b>	Prodrug. Aripiprazole undergoes hepatic metabolism by CYP2D6 & CYP3A4
<b>T<sub>max</sub></b>	~27 days (range: 16 to 35 days)

### Adverse Reactions

The most commonly observed adverse reaction (incidence  $\geq 5\%$  & at least twice that for placebo): Akathisia

Adverse Reaction in  $\geq 2\%$  & at Greater Incidence than in the Placebo-Treated Patients in the 12-Week Schizophrenia Trial

Adverse Reaction System Organ Class Preferred Term	Placebo N=207 (%)	Aripiprazole Lauroxil	
		441 mg N=207 (%)	882 mg N=208 (%)
<b>General disorders and administration site conditions</b>			
Injection site pain	2	3	4
<b>Investigations</b>			
Increased weight	1	2	2
Increased blood creatine phosphokinase	0	2	1
<b>Nervous system disorders</b>			
Akathisia	4	11	11
Headache	3	3	5
<b>Psychiatric disorders</b>			
Insomnia	2	3	4
Restlessness	1	3	1

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## **Role in Therapy**

- Aristada Initio appears to be effective, it offers a new initiation strategy for a long-acting treatment option for clients with schizophrenia
- the 1<sup>st</sup> long-acting aripiprazole regimen that can be initiated on the first day without oral therapy being continued post-initiation
  - a quicker time to therapeutic concentration, however
  - other LAI options available which do not require concurrent oral therapy (please see comparison table below)
  - Concerns about client's willingness to receive two injections on day one
    - Option to give the 1<sup>st</sup> Aristada injection within ten days of Aristada Initio administration
    - Option for re-initiation of Aristada without oral overlap
- Aristada Initio is available as a 675 mg single-dose strength only
  - dosage adjustments not possible
  - Concerns about DDIs, concomitant use with anti-hypertensive agents & benzos
- Aristada Initio may improve adherence, but like other LAI antipsychotics, its effects cannot be reversed if toxicity occur. Use of Aristada, may lead to side-effects like insomnia, akathisia, and headache

## **PA Approval Criteria**

- All medically accepted indications
- Patient has history of noncompliance with oral antipsychotics or difficulty in swallowing oral medications
- Approve one dose of Aristada Initio with oral Aripiprazole

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1. With the addition of the single Aristada Initio and a 30-mg oral aripiprazole with the 1<sup>st</sup> Aristada dose