Aripiprazole Lauroxil Extended-Release Injectable (Aristada®)
FDA Approved October 2015

Indication
Aristada is indicated for the treatment of schizophrenia

Mechanism
Aripiprazole lauroxil is a prodrug of aripiprazole. Aripiprazole functions as a partial agonist for serotonin 5-HT_{1A} and dopamine D_2 receptors and as an antagonist at serotonin 5-HT_{2A} receptors

Dosage & administration
- Establish tolerability with oral aripiprazole for 2 weeks before starting Aristada
- Administer oral aripiprazole for 21 days in conjunction with the first Aristada injection
- Use the following Aristada doses for patients stabilized on oral aripiprazole

Oral Aripiprazole Dose	Aristada IM Dose	Site of IM injection
10 mg a day	441 mg a month	Deltoid or Gluteal
15 mg a day	662 mg a month	Gluteal
20 mg or higher a day	882 mg a month or every 6 weeks	Gluteal

- Adjust dose as needed (consider the pharmacokinetics & prolonged-release characteristics). If a dose is required earlier than the recommended interval, do not administer <14 days after the previous injection
- No dosage adjustment necessary in renal or hepatic impairment

Dose Adjustments with Concomitant CYP450 Modulator Use
- Refer to oral aripiprazole prescribing information for the first 21 days concomitant use with Aristada
- Refer to recommendations below if CYP450 modulators are added for ≥2 weeks. No dosage adjustment necessary if CYP450 modulators are used for <2 weeks

Concomitant Medication	Dose Change for ARISTADA
Strong CYP3A4 Inhibitor	Reduce Aristada dose to the next lower strength* *For patients known to be poor metabolizers of CYP2D6:* Reduce dose to 441 mg regardless of the current dose. No dosage adjustment necessary if receiving 441 mg, if tolerated
Strong CYP2D6 Inhibitor	Reduce Aristada dose to the next lower strength* *For patients known to be poor metabolizers of CYP2D6 or if using Aristada 441 mg*: No dosage adjustment necessary, if tolerated
Both Strong CYP3A4 & CYP2D6 Inhibitor	Avoid use in patients receiving 662 mg or 882 mg dose. No dosage adjustment necessary if receiving 441 mg, if tolerated
CYP3A4 Inducer	No dose adjustment for 662 mg or 882 mg, increase the 441 mg dose to 662 mg

*In patients receiving 882 mg every 6 weeks, the next lower dose should be 441 mg every 4 weeks

Administration
- Administer via IM injection in the deltoid (441 mg dose only) or gluteal muscle over <10 seconds
- 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 (1 - 1.5 inch for deltoid & 1.5 - 2-inch for gluteal inj). Patients with a larger amount of subcutaneous tissue should use the longer of the needles provided

Pharmacokinetics

Onset of action	5 - 6 days following inj, 4 days when administered concomitantly with PO aripiprazole
Half-life elimination	29 to 35 days (oral aripiprazole: mean 75 hours)
Steady-state	steady state concentration reached following the 4th monthly injection
Duration of action	36 days following appearance in the systemic circulation
Metabolism	prodrug, aripiprazole undergoes hepatic metabolism by CYP2D6 & CYP3A4

Adverse Reactions: The most common adverse effects were akathisia, insomnia, and headache

Adverse Reaction in ≥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 (%)	Aripiprazole Lauroxil 882 mg N=208 (%)
General disorders and administration site conditions			
Injection site pain	2	3	4
Investigations			
Increased weight	1	2	2
Increased blood creatine phosphokinase	0	2	1
Nervous system disorders			
Akathisia	4	11	11
Headache	3	3	5
Psychiatric disorders			
Insomnia	2	3	4
Restlessness	1	3	1

Comparison with oral Aripiprazole & Abilify Maintena

	Aripiprazole oral	**Abilify Maintena IM**	**Aristada™ (aripiprazole lauroxil) IM**
FDA approved indications	Schizophrenia, Bipolar I disorder, MDD (adjunctive tt), Autism (treatment of irritability), Tourette disorder	Schizophrenia	Schizophrenia
Dosage Schizophrenia	Initial: 10 - 15 mg once daily Maximum: 30 mg once daily	• 400 mg once monthly • After initial injection, continue PO aripiprazole for *14 days*	• 441 - 882 mg IM once monthly. 882 mg dose may also be given Q 6 wks • After initial injection, continue PO aripiprazole for *21 days*
Available in	Tabs: 2, 5, 10, 15, 20, & 30 mg	Prefilled syringe & single-use vials: 300 mg, 400 mg	Prefilled syringe: 441 mg, 662 mg, 882 mg
Administration	Administer with or without food	• Reconstitution needed • Shake syringe vigorously for 20 sec, shake vials for 30 sec • Inject *slowly* into deltoid or gluteal muscle (300 or 400 mg)	• Reconstitution not needed • Tap 10 times, shake vigorously for 30 sec • Inject over *<10 seconds* into deltoid or gluteal muscle (441 mg), gluteal only (662 or 882 mg)
Half-life elimination	Aripiprazole:75 hr; dehydro-aripiprazole:94 hr	dose-dependent: 30 days (300 mg), 47 days (400 mg)	29 to 35 days (Q 4-week inj)
Steady-state conc		by the 4th dose	following the 4th monthly injection
Metabolism	Hepatic, via CYP2D6, CYP3A4	Hepatic, via CYP2D6, CYP3A4	Hepatic, via CYP2D6, CYP3A4 Prodrug, undergoes hydrolysis to form N-hydroxymethyl-aripiprazole & aripiprazole

Formulary status: PA required
Please contact BHRS Pharmacy Services for additional information

References available upon request