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

<table>
<thead>
<tr>
<th>Oral Aripiprazole Dose</th>
<th>Aristada IM Dose</th>
<th>Site of IM injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mg a day</td>
<td>441 mg a month</td>
<td>Deltoid or Gluteal</td>
</tr>
<tr>
<td>15 mg a day</td>
<td>662 mg a month</td>
<td>Gluteal</td>
</tr>
<tr>
<td>20 mg or higher a day</td>
<td>882 mg a month or every 6 weeks</td>
<td>Gluteal</td>
</tr>
</tbody>
</table>

- 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

<table>
<thead>
<tr>
<th>Pharmacokinetic Parameter</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Onset of action</strong></td>
<td>5 - 6 days following inj, 4 days when administered concomitantly with PO aripiprazole</td>
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<tr>
<td><strong>Half-life elimination</strong></td>
<td>29 to 35 days (oral aripiprazole: mean 75 hours)</td>
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<tr>
<td><strong>Steady-state</strong></td>
<td>steady state concentration reached following the 4th monthly injection</td>
</tr>
<tr>
<td><strong>Duration of action</strong></td>
<td>36 days following appearance in the systemic circulation</td>
</tr>
<tr>
<td><strong>Metabolism</strong></td>
<td>prodrug, aripiprazole undergoes hepatic metabolism by CYP2D6 &amp; CYP3A4</td>
</tr>
</tbody>
</table>

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

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

Comparison with oral Aripiprazole & Abilify Maintena

**FDA approved indications**
- Schizophrenia, Bipolar I disorder, MDD (adjunctive tt), Autism (treatment of irritability), Tourette disorder

**Dosage**
- **Schizophrenia**
  - Initial: 10 - 15 mg once daily
  - Maximum: 30 mg once daily
  - After initial injection, continue PO aripiprazole for 14 days
  - • 400 mg once monthly
  - • After initial injection, continue PO aripiprazole for 47 days (300 mg), 47 days (400 mg)

- **Abilify Maintena IM**
  - • 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**
- **Aripiprazole oral**
  - Tabs: 2, 5, 10, 15, 20, & 30 mg
- **Aristada™ (aripiprazole lauroxil) IM**
  - 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
- 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