Clinical Policy: Aripiprazole Long-Acting Injections (Abilify Maintena, Aristada)
Reference Number: ERX.SPA.177
Effective Date: 09.05.17
Last Review Date: 11.17
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Aripiprazole monohydrate (Abilify Maintena®) and aripiprazole lauroxil (Aristada®) are atypical antipsychotics.

FDA Approved Indication(s)
Abilify Maintena is indicated:
- For the treatment of schizophrenia in adults
- For maintenance monotherapy treatment of bipolar I disorder in adults

Aristada is indicated for the treatment of schizophrenia.

Policy/Criteria
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Abilify Maintena and Aristada are medically necessary when the following criteria are met:

I. Initial Approval Criteria
   A. Schizophrenia (must meet all):
      1. Diagnosis of schizophrenia;
      2. Prescribed by or in consultation with a psychiatrist;
      3. Age ≥ 18 years;
      4. History of non-adherence to oral antipsychotic therapy (see Appendix B);
      5. Established tolerability with oral aripiprazole;
      6. If request is for Abilify Maintena, failure of Risperdal Consta and Aristada, unless both are contraindicated or clinically significant adverse effects are experienced;
      7. Dose does not exceed the following (a or b):
         a. Abilify Maintena: 400 mg/month;
         b. Aristada: 882 mg/month.
   Approval duration: Length of Benefit

   B. Bipolar Disorder (must meet all):
      1. Diagnosis of bipolar disorder;
      2. Request is for Abilify Maintena;
      3. Prescribed by or in consultation with a psychiatrist;
      4. Age ≥ 18 years;
      5. History of non-adherence to oral antipsychotic therapy (see Appendix B);
      6. Established tolerability with oral aripiprazole;
      7. Failure of Risperdal Consta unless contraindicated or clinically significant adverse effects are experienced;
      8. Dose does not exceed 400 mg/month.
   Approval duration: Length of Benefit

   C. Other diagnoses/indications
      1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy
A. All Indications in Section I (must meet all):
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Abilify Maintena for schizophrenia or bipolar disorder, or Aristada for schizophrenia, and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed the following (a or b):
   a. Abilify Maintena: 400 mg/month;
   b. Aristada: 882 mg/month.

Approval duration: Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2):
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy. 
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:
A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents;
B. Dementia-related psychosis.

IV. Appendices/General Information
Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration

Appendix B: Examples of Oral Antipsychotics – Generic (Brand)

<table>
<thead>
<tr>
<th>Typical/First Generation Antipsychotics†</th>
<th>Atypical/Second Generation Antipsychotics</th>
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</thead>
<tbody>
<tr>
<td>Chlorpromazine (Thorazine)</td>
<td>Aripiprazole (Abilify)*</td>
</tr>
<tr>
<td>Fluphenazine (Prolixin)</td>
<td>Asenapine maleate (Saphris)</td>
</tr>
<tr>
<td>Haloperidol (Haldol)</td>
<td>Brexpiprazole (Rexulti)</td>
</tr>
<tr>
<td>Loxapine (Loxitane)</td>
<td>Cariprazine (Vraylar)</td>
</tr>
<tr>
<td>Perphenazine (Trilafon)</td>
<td>Clozapine (Clozaril)</td>
</tr>
<tr>
<td>Pimozide (Orap)</td>
<td>Iloperidone (Fanapt)</td>
</tr>
<tr>
<td>Thiordinazine (Mellaril)</td>
<td>Lurasidone (Latuda)</td>
</tr>
<tr>
<td>Thiothixene (Navane)</td>
<td>Olanzapine (Zyprexa)*</td>
</tr>
<tr>
<td>Trifluoperazine (Stelazine)</td>
<td>Olanzapine/fluoxetine (Symbyax)</td>
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<tr>
<td></td>
<td>Paliperidone (Invega)*</td>
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<tr>
<td></td>
<td>Quetiapine (Seroquel)</td>
</tr>
<tr>
<td></td>
<td>Risperidone (Risperdal)*</td>
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<td></td>
<td>Ziprasidone (Geodon)</td>
</tr>
</tbody>
</table>

†Most typical/first generation antipsychotics are available only as generics in the U.S.
*Long-acting injectable formulation available

Appendix C: Therapeutic Alternatives

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Dosing Regimen</th>
<th>Dose Limit/Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole (Abilify*)</td>
<td>Bipolar Disorder and Schizophrenia Adults: 10-15 mg PO QD</td>
<td>30 mg/day</td>
</tr>
<tr>
<td>Risperdal Consta® (risperidone)</td>
<td>Bipolar Disorder and Schizophrenia Adults: 25 mg IM every 2 weeks. Patients not responding to 25 mg may benefit from a higher dose of 37.5 mg or 50 mg.</td>
<td>50 mg every 2 weeks</td>
</tr>
</tbody>
</table>
Aripiprazole Long-Acting Injections

V. Dosage and Administration

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Indication</th>
<th>Dosing Regimen</th>
<th>Maximum Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole monohydrate (Abilify Maintena)</td>
<td>Schizophrenia</td>
<td>The recommended starting and maintenance dose is 400 mg IM monthly (no sooner than 26 days after the previous injection). Dose can be reduced to 300 mg in patients with adverse reactions.</td>
<td>400 mg/month</td>
</tr>
<tr>
<td></td>
<td>Bipolar I disorder</td>
<td>Known CYP2D6 poor metabolizers: Recommended starting and maintenance dose is 300 mg IM monthly as a single injection.</td>
<td></td>
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<tr>
<td>Aripiprazole lauroxil (Aristada)</td>
<td>Schizophrenia</td>
<td>Depending on individual patient’s needs, treatment can be initiated at a dose of 441 mg, 662 mg, or 882 mg IM administered monthly; 882 mg administered every 6 weeks; or 1064 mg administered every 2 months. Dose adjustments are required for 1) known CYP2D6 poor metabolizers and 2) for patients taking CYP3A4 inhibitors, CYP2D6 inhibitors, or CYP3A4 inducers for more than 2 weeks.</td>
<td>882 mg/month</td>
</tr>
</tbody>
</table>

VI. Product Availability

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole monohydrate (Abilify Maintena)</td>
<td>Extended-release injectable suspension (single-dose pre-filled dual chamber syringe and single-dose vial): 300 mg and 400 mg</td>
</tr>
<tr>
<td>Aripiprazole lauroxil (Aristada)</td>
<td>Extended-release injectable suspension (single-use pre-filled syringe): 441 mg, 662 mg, 882 mg, or 1064 mg</td>
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</tbody>
</table>

VII. References

Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Date</th>
<th>P&amp;T Approval Date</th>
</tr>
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<tr>
<td>09.05.17</td>
<td>11.17</td>
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4Q17 Annual Review
Policy split from ERX.SPMN.192 Long-acting injectable antipsychotics.
Converted to new template.
Added age restriction as safety and effectiveness have not been established in patients < 18 years.
Reviews, Revisions, and Approvals

<table>
<thead>
<tr>
<th>Added max dose. Increased all approval durations to length of benefit. Schizophrenia: Added a requirement related to trial and failure of Aristada (if request is for Abilify Maintena) since Aristada is another formulary agent indicated for schizophrenia. Removed “therapeutic plan includes an initial 14 days of concomitantly administered oral antipsychotic therapy with Abilify Maintena” and “therapeutic plan includes an initial 21 days of concomitantly administered oral aripiprazole therapy with Aristada” from initial approval criteria and similar drug-specific criteria related to treatment plan on re-auth since specialist is involved in care.</th>
<th>Date</th>
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</tr>
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Added new FDA approved indication for Abilify Maintena: bipolar I disorder.

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.

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