Clinical Policy: Aripiprazole Long-Acting Injection (Abilify Maintena, Aristada, Aristada Initio)

Reference Number: IL.ERX.SPA.177
Effective Date: 06.01.21
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Line of Business: Illinois Medicaid

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®, Aristada Initio™) 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.

Aristada Initio, in combination with oral aripiprazole, is indicated:
- For the initiation of Aristada when used for the treatment of schizophrenia in adults.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Abilify Maintena, Aristada, and Aristada Initio 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. Member meets one of the following (a or b):
   a. History of non-adherence to oral antipsychotic therapy (*see Appendix D for examples*) and established tolerability with oral aripiprazole;
   b. Therapy was initiated in an inpatient setting during a recent (within 60 days) hospital admission;
5. Dose does not exceed one of the following (a, b, or c):
   a. Abilify Maintena: 400 mg per month;
   b. Aristada: 882 mg per month, 882 mg per 6 weeks, or 1,064 mg per 2 months;
   c. Aristada Initio: 675 mg one-time dose *(used in conjunction with Aristada and an oral one-time 30 mg dose of aripiprazole)*.

Approval duration: 12 months

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. Member meets one of the following (a or b):
   a. History of non-adherence to oral antipsychotic therapy (*see Appendix D for examples*) and has established tolerability with oral aripiprazole;
   b. Therapy was initiated in an inpatient setting during a recent (within 60 days) hospital admission;
6. Dose does not exceed 400 mg per month.

Approval duration: 12 months

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 the following (a or b):
   a. Member is currently receiving the requested agent for a covered indication, and has received this medication for at least 30 days;
   b. Therapy was initiated in an inpatient setting for a covered indication during a recent (within 60 days) hospital admission;
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 per month;
   b. Aristada: 882 mg per month, 882 mg per 6 weeks, or 1,064 mg per 2 months.

Approval duration: 12 months

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: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
aripiprazole (Abilify®)	Bipolar Disorder and Schizophrenia Adults: 10-15 mg PO QD	30 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): none reported
- Boxed warning(s): increased mortality in elderly patients with dementia-related psychosis.

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

Typical/First Generation Antipsychotics†	Atypical/Second Generation Antipsychotics
• Chlorpromazine (Thorazine®) • Fluphenazine (Prolixin®) • Haloperidol (Haldol®) • Loxapine (Loxitane®) • Perphenazine (Trilafon®) • Pimozide (Orap®) • Thioridazine (Mellaril®) • Thiothixene (Navane®) • Trifluoperazine (Stelazine®)	• Aripiprazole (Abilify)* • Asenapine maleate (Saphris®) • Brexpiprazole (Rexulti®) • Cariprazine (Vraylar®) • Clozapine (Clozaril®) • Iloperidone (Fanapt®) • Lumateperone (Caplyta®) • Lurasidone (Latuda®) • Olanzapine (Zyprexa®)* • Olanzapine/fluoxetine (Symbyax®) • Paliperidone (Invega®)* • Quetiapine (Seroquel®) • Risperidone (Risperdal®)* • Ziprasidone (Geodon®)

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

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Aripiprazole monohydrate (Abilify Maintena)	Schizophrenia Bipolar I disorder	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. • Used in combination with oral aripiprazole for the first 14 consecutive days. • Known CYP2D6 poor metabolizers: Recommended starting and maintenance dose is 300 mg IM monthly as a single injection.	400 mg/month
Aripiprazole lauroxil (Aristada)	Schizophrenia	*Initiation Method 1*: Administer one IM injection of Aristada Initio 675 mg (deltoid or gluteal muscle) and one dose of oral aripiprazole 30mg in conjunction with the first Aristada injection. • First Aristada injection may be started on same day or up to 10 days after administration of Aristada Initio • Avoid injection of both Aristada and Aristada Initio into the same deltoid or gluteal muscle. *Initiation Method 2:* Used in combination with oral aripiprazole for the first 21 consecutive days. Depending on individual patient's needs, treatment can be initiated at a dose of 441 mg, 662 mg, or 882 mg IM administered	882 mg/month

Drug Name	Indication	Dosing Regimen	Maximum Dose
		monthly; 882 mg administered every 6 weeks; or 1,064 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.	
Aripiprazole lauroxil (Aristada Initio)	Schizophrenia *(therapy initiation only)*	Single dose of 675 mg IM injection, in combination with a single dose of 30 mg oral aripiprazole, to initiate Aristada treatment or to re-initiate Aristada treatment. Aristada may be started at the same time or within 10 days of Aristada Initio/oral aripiprazole.	675 mg once

VI. Product Availability

Drug Name	Availability
Aripiprazole monohydrate (Abilify Maintena)	Extended-release injectable suspension (single-dose pre-filled dual chamber syringe and single-dose vial): 300 mg and 400 mg
Aripiprazole lauroxil (Aristada)	Extended-release injectable suspension (single-use pre-filled syringe): 441 mg, 662 mg, 882 mg, or 1,064 mg
Aripiprazole lauroxil (Aristada Initio)	Extended-release injectable suspension (single-use pre-filled syringe): 675 mg

VII. References

1. Abilify Maintena Prescribing Information. Rockville, MD: Otsuka America Pharmaceutical, Inc.; January 2020. Available at https://www.abilifymaintena.com/. Accessed March 19, 2021.
2. Aristada Prescribing Information. Waltham, MA: Alkermes, Inc.; February 2020. Available at https://www.aristada.com. Accessed March 19, 2021.
3. Aristada Initio Prescribing Information. Waltham, MA: Alkermes, Inc.; February 2020. Available at https://www.aristada.com/downloadables/ARISTADA-INITIO-PI.pdf. Accessed March 19, 2021.
4. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2020. Available at: http://www.clinicalpharmacology-ip.com/. Accessed March 19, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	04.23.21	05.21
3Q 2021 annual review: added initial and continued criteria for either history of non-adherence to PO antipsychotic therapy or therapy initiated recently in an inpatient setting; references reviewed and updated.	07.16.21	08.21

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.