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

Reference Number: CP.PHAR.290
Effective Date: 12.01.16
Last Review Date: 08.22
Line of Business: HIM, Medicaid

Coding Implications
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 in adults

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.

It is the policy of health plans affiliated with Centene Corporation® 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 has established tolerability to oral aripiprazole;
   b. Therapy was initiated in an inpatient setting during a recent (within 60 days) hospital admission;
5. Dose does not exceed 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: 6 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 to 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: 6 months

C. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Member meets one of the following (a, b, or c):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
   c. 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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: HIM.PA.33 for health insurance marketplace and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: HIM.PA.103 for health insurance marketplace and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

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 policies – CP.PMN.53 for Medicaid and HIM.PA.154 for health insurance marketplace, 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 for all relevant lines of business 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): known hypersensitivity to aripiprazole
- 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	882 mg/month

Drug Name	Indication	Dosing Regimen	Maximum Dose
		• 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 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.	
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 powder for suspension for injection (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/1.6 mL, 662 mg/2.4 mL, 882 mg/3.2 mL or 1,064 mg/3.9 mL
Aripiprazole lauroxil (Aristada Initio)	Extended-release injectable suspension (single-use pre-filled syringe): 675 mg/2.4 mL

VII. References

1. Abilify Maintena Prescribing Information. Rockville, MD: Otsuka America Pharmaceutical, Inc.; January 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/202971s013lbl.pdf. Accessed May 12, 2022.
2. Aristada Prescribing Information. Waltham, MA: Alkermes, Inc.; February 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/207533s017,209830s005lbl.pdf. Accessed May 12, 2022.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2022. Available at: http://www.clinicalpharmacology-ip.com/. Accessed May 12, 2022.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0401	Injection, aripiprazole, extended release, 1 mg
J1943	Injection, aripiprazole lauroxil, (aristada initio), 1 mg
J1944	Injection, aripiprazole lauroxil, (aristada), 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2018 annual review: no significant changes; references reviewed and updated	05.01.18	08.18
No significant changes: new formulation added (Aristada Initio).	07.31.18	
Initial and continued therapy criteria were revised to allow approval for members who initiated therapy during a recent inpatient visit, without the requirement to step through oral agents.	02.26.19	02.19
3Q 2019 annual review: no significant changes; added HIM-Medical Benefit lines of business; added boxed warning; updated dosage and administration in accordance with label changes; references reviewed and updated.	05.24.19	08.19
3Q 2020 annual review: no significant changes; revised HIM-Medical Benefit to HIM line of business; references reviewed and updated.	05.12.20	08.20
3Q 2021 annual review: no significant changes; updated reference for HIM off-label use to HIM.PA.154 (replaces HIM.PHAR.21); references reviewed and updated.	03.19.21	08.21
3Q 2022 annual review: no significant changes; references reviewed and updated.	05.12.22	08.22
Template changes applied to other diagnoses/indications and continued therapy section.	09.20.22	

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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members

and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.