

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

Reference Number: IL.PHAR.290

Effective Date: 1.1.20

Last Review Date: 9.8.21

[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.

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, Schizoaffective Disorder (must meet all):

1. Documented diagnosis of schizophrenia or schizoaffective disorder;
2. Prescribed by or in consultation with a psychiatrist;
3. Age \geq 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. Prescribed dose does not exceed the following (a or b):
 - a. If request is for Abilify Maintena, dose does not exceed 400 mg monthly;
 - b. If request is for Aristada, dose does not exceed 882 mg (delivers a dose of 600 mg aripiprazole) monthly; 882 mg per 6 weeks, or 1064 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 \geq 18 years; 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 400 mg per month.

Approval duration: 6 months

C. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy; or
2. Refer to CP.PHAR.53 - No Coverage Criteria/Off-Label Use Policy.

II. Continued Therapy

A. All Indications in Section I (must meet all):

1. Currently receiving medication via Centene benefit, or documentation supports one of 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 1064 mg per 2 months.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): 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 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): 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
<ul style="list-style-type: none"> • Chlorpromazine (Thorazine®) • Fluphenazine (Prolixin®) • Haloperidol (Haldol®) • Loxapine (Loxitane®) • Perphenazine (Trilafon®) • Pimozide (Orap®) • Thioridazine (Mellaril®) • Thiothixene (Navane®) • Trifluoperazine (Stelazine®) 	<ul style="list-style-type: none"> • 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	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.	400 mg/month
	Bipolar I disorder	<ul style="list-style-type: none"> • 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. 	
Aripiprazole lauroxil (Aristada)	Schizophrenia	<p><i>Initiation Method 1:</i> 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.</p> <ul style="list-style-type: none"> • 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. <p><i>Initiation Method 2:</i> Used in combination with oral aripiprazole for the first 21 consecutive days.</p> <p>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.</p> <p>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.</p>	882 mg/month

Drug Name	Indication	Dosing Regimen	Maximum Dose
Aripiprazole lauroxil (Aristada Initio)	Schizophrenia (<i>therapy initiation only</i>)	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 1064 mg
Aripiprazole lauroxil (Aristada Initio)	Extended-release injectable suspension (single-use pre-filled syringe): 675 mg

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
C9470	Injection, aripiprazole lauroxil, 1 mg
J0401	Injection, aripiprazole, extended release, 1 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.; 2021. Available at: <http://www.clinicalpharmacology-ip.com/>. Accessed March 19, 2021.

Reviews, Revisions, and Approvals	Date	Approval Date
Added schizoaffective disorder as approvable diagnosis. Removed requirement on prescriber specialty, removed requirement for nonadherence to oral antipsychotic therapy and established tolerability with oral aripiprazole. Removed requirement for initial concomitant use of oral antipsychotic therapy. Extended initial approval to 12 months and removed criteria for continued approval.	11/17	11/17
Policy split from CP.PHAR.122.LAI Antipsychotics and converted to new template. Age removed and max dose added per template guidelines. Hypersensitivity contraindication added. Appendix B: Oral Antipsychotics – reviewed, edited and updated per UpToDate and FDA websites (7-9). Specialist review by psychiatrist.	11/16	12/16
Added language to support migration to HFS PDL.	12.10 .19	1.7.20
Added criteria for bipolar diagnosis	1.7.2 0	
2Q 2021 Annual review: Removed Criteria No history of dementia-related psychosis; Member has no known hypersensitivity to aripiprazole (e.g., pruritus/urticaria, anaphylaxis); For schizophrenia criteria: added age ≥ 18; added prescriber requirement; added Hx of non-adherence, tolerability to oral, and initiated in an inpatient setting; added Aristada Initio; For bipolar criteria: added prescriber requirement; added Hx of non-adherence, tolerability to oral, and initiated in an inpatient setting; Added Dosage and Administration; updated product availability; added <i>Appendix C: Contraindications / Boxed warnings</i> ; reviewed and updated references	6.17. 21	
3Q 2021 annual review: no significant changes; references reviewed and updated.	9.8.2 1	

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.

CLINICAL POLICY

Aripiprazole Long-Acting Injections



“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.

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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.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

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