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

Reference Number: IL.PHAR.290
Effective Date: 1.1.20
Last Review Date: 1.19.24

Coding Implications
Revision Log

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

Description

Aripiprazole monohydrate (Abilify Maintena®, Abilify Asimtufii®) and aripiprazole lauroxil (Aristada®, Aristada Initio®) are atypical antipsychotics.

FDA Approved Indication(s)

Abilify Maintena and Abilify Asimtufii are 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, Abilify Asimtufii, 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 ≥ 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. The prescriber agrees to coordinate a follow up outpatient appointment for administration of the next recommended dose of the LAI atypical antipsychotic agents and provide documentation of the follow up appointment with request for prior approval.
6. Dose does not exceed any of the following (a, b, c, or d):

a. Abilify Maintena: 400 mg per month;
b. Abilify Asimtufii: 960 mg per 2 months;
c. Aristada (i, ii, or iii):
   i. 882 mg per month;
   ii. 882 mg per 6 weeks;
   iii. 1,064 mg per 2 months;
d. 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 or Abilify Asimtufii;;
3. Prescribed by or in consultation with a psychiatrist;
4. Age ≥ 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. The prescriber agrees to coordinate a follow up outpatient appointment for administration of the next recommended dose of the LAI atypical antipsychotic agents and provide documentation of the follow up appointment with request for prior approval.
6. Dose does not exceed any of the following (a or b):
   5) Abilify Maintena: 400 mg per month;
   6) Abilify Asimtufii: 960 mg per 2 months.

Approval duration: 12 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 (health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: 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: CP.PMN.53 for Medicaid.

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 Abilify Maintena, Abilify Asimtufii, or Aristada for bipolar disorder or schizophrenia 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 any of the following (a, b, or c):
   a. Abilify Maintena: 400 mg per month;
   b. Abilify Asimtufii: 960 mg per 2 months;
   c. Aristada (i, ii, or iii):
      i. 882 mg per month;
      ii. 882 mg per 6 weeks;
      iii. 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 (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 (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 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
• 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,	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

Drug Name	Indication	Dosing Regimen	Maximum Dose
	bipolar I disorder	• 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 monohydrate (Abilify Asimtufii)	Schizophrenia, bipolar I disorder	The recommended dose is 960 mg IM once every 2 months (56 days after the previous injection). Dose can be reduced to 720 mg in patients with adverse reactions. • Patients receiving oral antipsychotics: Administer the first dose of Abilify Asimtufii along with oral aripiprazole or another oral antipsychotic (and known to tolerate aripiprazole) for 14 consecutive days. • Patients receiving Abilify Maintena: Administer Abilify Asimtufii 960 mg IM (once every 2 months as a single injection) in place of the next scheduled injection of the Abilify Maintena. • Known CYP2D6 poor metabolizers: Recommended dose is 720 mg IM once every 2 months as a single injection.	960 mg/2 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:*	882 mg/month

Drug Name	Indication	Dosing Regimen	Maximum Dose
		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 syringes and single-dose vials): 300 mg and 400 mg
Aripiprazole monohydrate (Abilify Asimtufii)	Extended-release injectable suspension (single-dose pre-filled syringes): 720 mg/2.4 mL, 960 mg/3.2 mL
Aripiprazole lauroxil (Aristada)	Extended-release injectable suspension (single-use pre-filled syringes): 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

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

VII. References

1. Abilify Maintena Prescribing Information. Rockville, MD: Otsuka America Pharmaceutical, Inc.; June 2020. Available at: https://www.abilifymaintenahcp.com/. Accessed May 9, 2023.
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3. Aristada Initio Prescribing Information. Waltham, MA: Alkermes, Inc.; March 2021. Available at: https://www.aristada.com/. Accessed May 9, 2023.
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6. Keepers G, Fochtmann L, Anzia J, et al. American Psychiatric Association practice guideline for the treatment of patients with schizophrenia, third edition (2020). Available at: https://psychiatryonline.org/doi/10.1176/appi.books.9780890424841. Accessed May 8, 2023.
7. McDonagh MS, Dana T, Selph S, Devine EB, et al. Treatments for schizophrenia in adults: A systematic review. Comparative Effectiveness Review No. 198. (Prepared by the Pacific Northwest Evidence-based Practice Center under Contract No. 290-2015-00009-I.) AHRQ Publication No. 17(18)-EHC031-EF. Rockville, MD: Agency for Healthcare Research and Quality; October 2017.
8. Hirschfield RMA, Bowden CL, Gitlin MJ, et al. American Psychiatric Association practice guideline for the treatment of patients with bipolar disorder, second edition (2010). Available at: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/bipolar.pdf. Accessed May 8, 2023.
9. Butler M, Urosevic S, Desai P, et al. Treatment for bipolar disorder in adults: A systematic review. Comparative Effectiveness Review No. 208. (Prepared by the Minnesota Evidence-based Practice Center under Contract No. 290-2012-00016-I.) AHRQ Publication No. 18-EHC012-EF. Rockville, MD: Agency for Healthcare Research and Quality; August 2018.

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	1.7.20	
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 *Appendix C: Contraindications / Boxed warnings;* reviewed and updated references	6.17.21	
3Q 2021 annual review: no significant changes; references reviewed and updated.	9.8.21	
1Q 2024 Annual Review: Template changes applied to other diagnoses/indications and continued therapy section. Initial approval criteria updated to reflect HFS policy; dosage administration and dose, and product availability updated; added newly approved formulation Abilify Asimtufii to the policy. references reviewed and updated.	1.19.24	

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.

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.