Clinical Policy: Aripiprazole for Oral Use (Abilify), Aripiprazole Tablets with Sensor (Abilify Mycite)

Reference Number: ERX.NPA.07
Effective Date: 07.01.15
Last Review Date: 02.22
Line of Business: Commercial, Medicaid

Revision Log

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

Description
Aripiprazole (Abilify®) is an atypical antipsychotic. Abilify Mycite® is a drug-device combination product comprised of aripiprazole tablets embedded with an Ingestible Event Marker (IEM) sensor intended to track drug ingestion.

FDA Approved Indication(s)
The oral formulations of Abilify are indicated:
- For the treatment of schizophrenia
- For the acute treatment of manic and mixed episodes associated with bipolar I disorder
- For the adjunctive treatment of major depressive disorder (MDD)
- For the treatment of irritability associated with autistic disorder
- For the treatment of Tourette's disorder

Abilify Mycite is indicated:
- For the treatment of schizophrenia in adults
- For the acute treatment of manic and mixed episodes associated with bipolar I disorder in adults as monotherapy or as adjunct to lithium or valproate
- For the maintenance treatment of bipolar I disorder in adults as monotherapy or as adjunct to lithium or valproate
- For the adjunctive treatment of MDD 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 and Abilify Mycite are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Schizophrenia (must meet all)**:**
1. Diagnosis of schizophrenia;
2. Age ≥ 13 years;
3. Member meets one of the following (a or b):
   a. Failure of two of the following generic atypical antipsychotics at up to maximally indicated doses, each used for ≥ 4 weeks unless clinically significant adverse effects are experienced or all are contraindicated: risperidone, quetiapine, olanzapine, ziprasidone;
   b. Member has diabetes mellitus or body mass index (BMI) > 30;
4. Dose does not exceed 30 mg per day.

Approval duration:
Commercial – Length of Benefit
Medicaid – 12 months

B. Bipolar Disorder (must meet all)**:**
1. Diagnosis of bipolar disorder;
2. Age ≥ 10 years;
3. Failure of lithium or valproic acid, unless clinically significant adverse effects are experienced or both are contraindicated;
4. Member meets one of the following (a or b):
   a. Failure of a ≥ 4-week trial of one of the following generic atypical antipsychotics at up to maximally indicated doses, unless clinically significant adverse effects are experienced or all are contraindicated: risperidone, quetiapine, olanzapine, ziprasidone;
   b. Member has diabetes mellitus or BMI > 30;
5. Dose does not exceed 30 mg per day.

Approval duration:
Commercial – Length of Benefit
Medicaid – 12 months

C. Major Depressive Disorder (must meet all)**:**
1. Diagnosis of MDD;
2. Age ≥ 18 years;
3. Failure of two antidepressants (e.g., selective serotonin reuptake inhibitor [SSRI], serotonin-norepinephrine reuptake inhibitor [SNRI], tricyclic antidepressant [TCA], bupropion, mirtazapine) from different classes at up to maximally indicated doses, each used for ≥ 4 weeks, unless member is unable to satisfy this requirement due to contraindications or clinically significant adverse effects to multiple antidepressants;
4. Aripiprazole is prescribed concurrently with an antidepressant;
5. Dose does not exceed 15 mg per day.

Approval duration:
Commercial – Length of Benefit
Medicaid – 12 months

D. Tourette's Disorder (must meet all)**:**
1. Diagnosis of Tourette's disorder;
2. Request is for an oral aripiprazole product other than Abilify Mycite;
3. Age between 6 and 18 years;
4. Failure of haloperidol or risperidone, unless clinically significant adverse effects are experienced or both are contraindicated;
5. Dose does not exceed:
   a. Weight < 50 kg: 10 mg per day;
   b. Weight ≥ 50 kg: 20 mg per day.

Approval duration:
Commercial – Length of Benefit
Medicaid – 12 months

E. Autistic Disorder (must meet all)**:**
1. Diagnosis of autistic disorder;
2. Request is for an oral aripiprazole product other than Abilify Mycite;
3. Prescribed by or in consultation with a mental health provider;
4. Age between 6 and 17 years;
5. Member meets one of the following (a or b):
   a. Failure of a ≥ 4-week trial of risperidone at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
   b. Member has diabetes mellitus or BMI > 30;
6. Dose does not exceed 15 mg per day.

Approval duration:
Commercial – Length of Benefit
Medicaid – 12 months

F. 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. Member meets one of the following (a or b):
   a. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
   b. Documentation supports that member is currently receiving Abilify or Abilify Mycite for schizophrenia or bipolar disorder 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 any of the following (a, b, or c):
   a. Schizophrenia, bipolar disorder: 30 mg per day;
   b. Major depressive disorder, autistic disorder: 15 mg per day;
   c. Tourette's disorder (i or ii):
      i. Weight < 50 kg: 10 mg per day;
      ii. Weight ≥ 50 kg: 20 mg per day.

Approval duration:
Commercial – Length of Benefit
Medicaid – 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 12 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.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

BMI: body mass index
FDA: Food and Drug Administration
MDD: major depressive disorder
SNRI: serotonin-norepinephrine reuptake inhibitor
SSRI: selective serotonin reuptake inhibitor
TCA: tricyclic antidepressant

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
Antipsychotics		
olanzapine (Zyprexa®)	**Schizophrenia** Initial: 5-10 mg PO QD; target: 10 mg PO QD **Bipolar Disorder** Monotherapy: 10-15 mg PO QD; adjunct to lithium or valproate: 10 mg PO QD	20 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
risperidone (Risperdal®)	**Schizophrenia** Initial: 1 mg PO BID or 2 mg PO QD; target: 4-8 mg PO QD **Bipolar Disorder** 2-3 mg PO QD **Tourette's Syndrome*** 0.5 mg/day PO with titrated based on response and tolerability **Autistic Disorder** Weight ≥ 20 kg: initial: 0.5 mg PO QD for at least 14 days; target: 1 mg PO QD Weight 15-19 kg: initial: 0.25 mg PO QD for at least 4 days; target: 0.5 mg PO QD	Schizophrenia Adolescents: 6 mg/day Adults: 16 mg/day Bipolar Disorder, Tourette's Syndrome* 6 mg/day Autistic Disorder 3 mg/day
quetiapine (immediate-release) (Seroquel®)	**Schizophrenia** Initial: 25 mg PO BID; target: 400-800 mg/day **Bipolar Disorder** Initial: 50 mg PO BID; target: 400-800 mg/day	800 mg/day
ziprasidone (Geodon®)	**Schizophrenia** 20 mg PO BID **Bipolar Disorder** Initial: 40 mg PO BID; target: 40-80 mg PO BID	160 mg/day
haloperidol (Haldol®)	**Tourette's Disorder** Adults: initial: 0.5-2 mg PO BID-TID; increase as needed (average dose: 15 mg/day) Adolescents: initial: 0.25-0.5 mg/day PO; usual range: 1-4 mg/day	Adults and adolescents > 40 kg: 100 mg/day Adolescents ≤ 40 kg: 15 mg/day
Selective Serotonin Reuptake Inhibitors (SSRIs)		
citalopram (Celexa®)	**Major Depressive Disorder** Refer to prescribing information	40 mg/day
escitalopram (Lexapro®)		20 mg/day
fluoxetine (Prozac®)		Immediate-release: 80 mg/day (20 mg/day if pediatric) Delayed-release: 90 mg/week
fluvoxamine* (immediate-release) (Luvox®)		150 mg/day
paroxetine (Paxil®, Paxil CR®, Pexeva®)		Immediate-release: 50 mg/day (40 mg/day if geriatric) Extended-release: 62.5 mg/day (50 mg/day if geriatric)

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
sertraline (Zoloft®)		200 mg/day (20 mg/day if age 6-11 years*)
Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)		
desvenlafaxine (Pristiq®)	**Major Depressive Disorder** Refer to prescribing information	400 mg/day
duloxetine (Cymbalta®)		120 mg/day
Fetzima® (levomilnacipran)		120 mg/day
venlafaxine (Effexor®, Effexor XR®)		Extended-release: 225 mg/day
Tricyclic Antidepressant (TCAs)		
amitriptyline (Elavil®)	**Major Depressive Disorder** Refer to prescribing information	150 mg/day
amoxapine		400 mg/day (300 mg/day if geriatric)
clomipramine* (Anafranil®)		250 mg/day (200 mg/day if pediatric)
desipramine (Norpramin®)		300 mg/day (100 mg/day if pediatric)
doxepin (Sinequan®)		300 mg/day
imipramine HCl (Tofranil®)		200 mg/day (150 mg/day if geriatric or pediatric)
imipramine pamoate (Tofranil PM®)		200 mg/day (100 mg/day if geriatric or pediatric)
nortriptyline (Pamelor®)		150 mg/day
protriptyline (Vivactil®)		60 mg/day (30 mg/day if geriatric or pediatric)
trimipramine (Surmontil®)		200 mg/day (100 mg/day if geriatric or pediatric)
Monoamine Oxidase Inhibitors		
isocarboxazid (Marplan®)	**Major Depressive Disorder** Refer to prescribing information	60 mg/day
phenelzine (Nardil®)		90 mg/day
selegiline (EMSAM® transdermal; Eldepryl®, Zelapar®, Carbex®)		Transdermal: 12 mg/24 hr Oral*: 30 mg/day
tranylcypromine (Parnate®)		60 mg/day
Other Antidepressants		
bupropion (Aplenzin®, Budeprion SR® , Budeprion XL®, Forfivo XL®, Wellbutrin®, Wellbutrin SR®, Wellbutrin XL®)	**Major Depressive Disorder** Refer to prescribing information	Immediate-release: 450 mg/day (300 mg/day if pediatric) Sustained-release: 400 mg/day Extended-release (HCl): 450 mg/day Extended-release (HBr): 522 mg/day
mirtazapine (Remeron®)		45 mg/day
perphenazine/ amitriptyline (Triavil®)		16 mg/day perphenazine and 200 mg/day amitriptyline
maprotiline (Ludiomil®)		150 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
nefazodone (Serzone®)		600 mg/day
trazodone (Desyrel®, Oleptro®)		Immediate-release: 400 mg/day Extended-release: 375 mg/day
vortioxetine (Trintellix®)		20 mg/day
vilazodone (Viibryd®)		40 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.
**Off-label*

V. Dosage and Administration

Indication	Dosing Regimen**	Maximum Dose
Schizophrenia	Adults: 10 to 15 mg PO QD Adolescents: initial: 2 mg PO QD; target: 10 mg PO QD	30 mg/day
Bipolar mania	Adults, as monotherapy: 15 mg PO QD Adults, as adjunct to lithium or valproate: 10 to 15 mg PO QD Pediatric, as monotherapy or as an adjunct to lithium or valproate: initial: 2 mg PO QD; target: 10 mg PO QD	30 mg/day
Major depressive disorder	Adults, as adjunct to antidepressants: initial: 2 to 5 mg PO QD; target: 5 to 10 mg PO QD	15 mg/day
Irritability associated with autistic disorder	Pediatric: initial: 2 mg PO QD; target: 5 to 10 mg PO QD	15 mg/day
Tourette's disorder	Weight < 50 kg: initial: 2 mg PO QD; target: 5 mg PO QD Weight ≥ 50 kg: initial: 2 mg PO QD; target: 10 mg PO QD	Weight < 50 kg: 10 mg/day Weight ≥ 50 kg: 20 mg/day

***Known CYP2D6 poor metabolizers: half of the usual dose*

VI. Product Availability

- Tablets: 2 mg, 5 mg, 10 mg, 15 mg, 20 mg, 30 mg
- Orally disintegrating tablets: 10 mg, 15 mg
- Oral solution: 1 mg/mL
- Tablets with sensor: 2 mg, 5 mg, 10 mg, 15 mg, 20 mg, 30 mg

VII. References

1. Abilify Prescribing Information. Tokyo, Japan: Otsuka America Pharmaceutical, Inc; June 2020. Available at: http://abilify.com/. Accessed November 13, 2021.
2. Abilify Mycite Prescribing Information. Tokyo, Japan: Otsuka America Pharmaceutical, Inc.; December 2020. Available at: http://abilifymycite.com/. Accessed November 13, 2021.
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7. Lehman AF, Lieberman JA, Dixon LB, et al. Practice guideline for the treatment of patients with schizophrenia, second edition. Arlington, VA: American Psychiatric Association; February 2004. Available online at http://www.psychiatryonline.org/guidelines. Accessed November 30, 2019.
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9. Murphy TK, Lewin AB, Storch EA, Stock S, and the American Academy of Child and Adolescent Psychiatry (AACAP) Committee on Quality Issues (CQI). Practice parameter for the assessment and treatment of children and adolescents with tic disorders. J Am Acad Child Adolesc Psychiatry. 2013; 52(12): 1341-1359.
10. Volkmar F, Siegel M, Woodbury-Smith M, et al. Practice parameter for the assessment and treatment of children and adolescents with autism spectrum disorder. J Am Acad Child Adolesc Psychiatry 2014; 53: 237.
11. Keepers G, Fochtmann L, Anzia J, et al. APA Practice guideline for the treatment of patients with schizophrenia, third edition. Am J Psychiatry. 2020 Sept;177(9):868-872.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q18 annual review: Removed BBW criteria of "Member does not have dementia-related psychosis"; Continued approval: removed depression/Tourette's/autism as COC diagnoses; No significant changes, References reviewed and updated.	02.05.18	02.18
1Q 2019 annual review: no significant changes; revised approval duration to length of benefit; references reviewed and updated.	10.30.18	02.19
RT4: Abilify Mycite added.	06.21.19	
1Q 2020 annual review: no significant changes; added Medicaid line of business with 12 month approval durations; references reviewed and updated.	11.30.19	02.20
1Q 2021 annual review: no significant changes; references reviewed and updated.	12.03.20	02.21
1Q 2022 annual review: no significant changes; specified that for autism and for Tourette's disorder, the request is not for Abilify Mycite since Mycite is not FDA-approved for these two indications; references reviewed and updated.	11.13.21	02.22

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.

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.