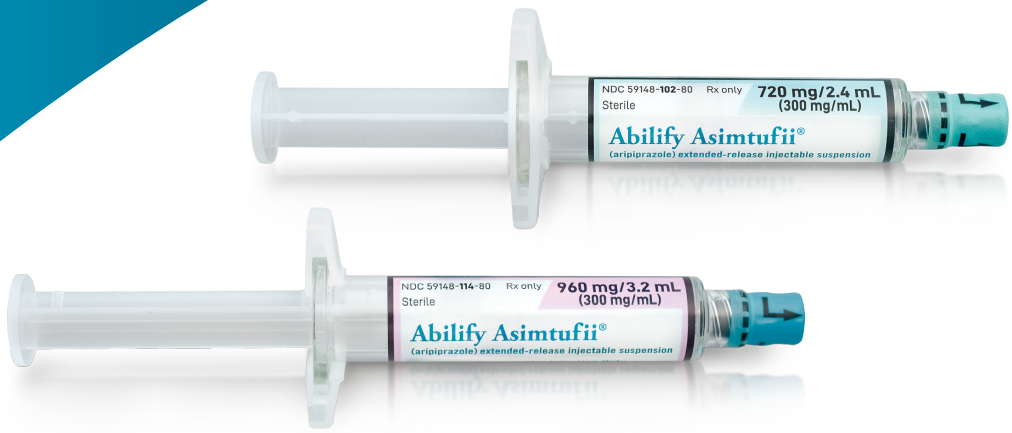
TRANSFORMING TREATMENT
FROM ORAL TO INJECTABLE

960MG
Abilify Asimtufii®
(aripiprazole) extended release suspension for injection



INDICATIONS and IMPORTANT SAFETY INFORMATION for ABILIFY ASIMTUFII® (aripiprazole)

INDICATIONS

ABILIFY ASIMTUFII® (aripiprazole) is an atypical antipsychotic indicated for:

- Treatment of schizophrenia in adults
- Maintenance monotherapy treatment of bipolar I disorder in adults

IMPORTANT SAFETY INFORMATION WARNING: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA RELATED PSYCHOSIS

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at increased risk of death (1.6 to 1.7 times) compared to placebo-treated patients. ABILIFY ASIMTUFII is not approved for the treatment of patients with dementia-related psychosis.

Please see **IMPORTANT SAFETY INFORMATION**, including **BOXED WARNING**, on pages 5 and 6.

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According to the National Council for Mental Wellbeing, patients who are currently on an oral antipsychotic can benefit from transitioning to an LAI. Clinicians may consider LAIs for patients who[1]

- Have difficulty adhering to oral medications
- Are not responding well to oral antipsychotics
- Are concerned about the social stigma of taking pills
- Have unstable living conditions
- Want fewer medications daily
- Prefer using an LAI

Initiating conversations about LAIs and using a shared decision-making approach with patients early in the treatment process may help inform the patient of their treatment options.[2] Shared-decision making has a positive impact on[3-5]:

Treatment adherence

Satisfaction with treatment

Patient empowerment

Before initiating treatment with an LAI, keep in mind[2]*

Previous response to specific antipsychotics and notable side effects

Dosing intervals

Expectations for tolerability and efficacy

Site of injection

Potential side effects

Out-of-pocket expenses

*From survey administered by Otsuka and Lundbeck to 42 expert researchers and prescribers.

The recommended dosage of ABILIFY ASIMTUFII® (aripiprazole):

ABILIFY ASIMTUFII
960 mg

Administered once every 2 months—
56 days ± 14 days after previous injection

If a patient is new to aripiprazole, tolerability must be established before initiating treatment with ABILIFY ASIMTUFII. Due to the half-life of oral aripiprazole, this may take up to 2 weeks.

Initiating ABILIFY ASIMTUFII

>> From any oral antipsychotic (patient is naïve to aripiprazole)

Establish tolerability with oral aripiprazole → **Initial dose of ABILIFY ASIMTUFII 960 mg** + **Continue current oral antipsychotic* for 14 consecutive days**

>> From any oral antipsychotic (patient has taken/tolerates aripiprazole)

Initial dose of ABILIFY ASIMTUFII 960 mg + **Continue current oral antipsychotic* for 14 consecutive days**

Once every 2 months:

56 days **± 14 days** after previous injection of ABILIFY ASIMTUFII 960 mg

Administer ABILIFY ASIMTUFII by intramuscular injection in the gluteal muscle by a healthcare professional. **Do not administer by any other route**. If there are adverse reactions with the ABILIFY ASIMTUFII 960 mg dosage, the dosage may be reduced to 720 mg once every 2 months.
*Oral aripiprazole (10 mg to 20 mg) or current oral antipsychotic.

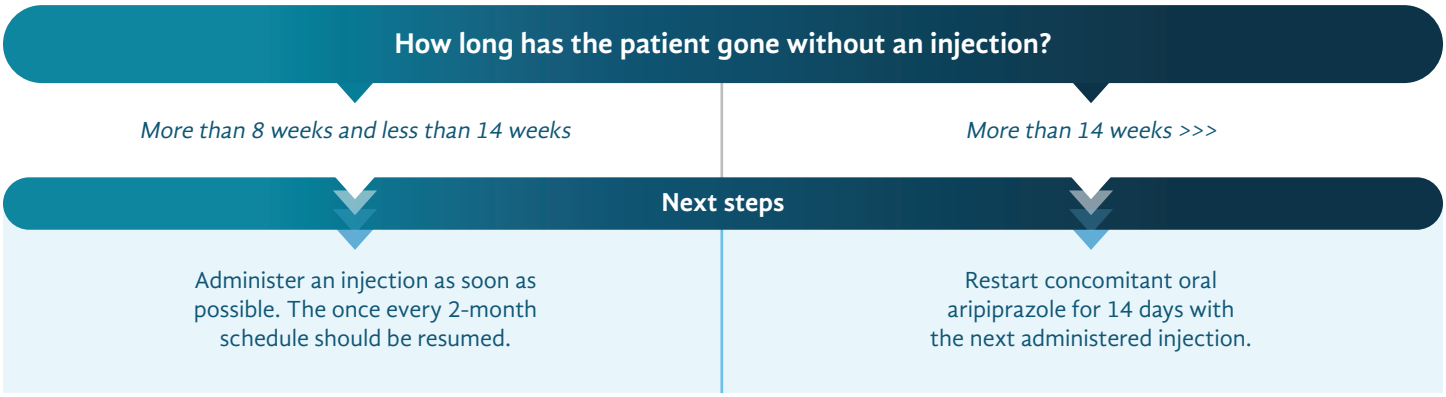
Contraindication
Known hypersensitivity reaction to aripiprazole. Reactions have ranged from pruritus/urticaria to anaphylaxis.

Important Warning and Precaution for Cerebrovascular Adverse Events, Including Stroke
Increased incidence of cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, have been reported in clinical trials of elderly patients with dementia-related psychosis treated with oral aripiprazole.

Please see **IMPORTANT SAFETY INFORMATION**, including the **BOXED WARNING**, on pages 5 and 6.

Patients may be given the ABILIFY ASIMTUFII® (aripiprazole) injection up to 2 weeks before or 2 weeks after the 2-month scheduled timepoint.

Recommendations for missed doses



Dosage adjustments can be made for patients who are CYP2D6 poor metabolizers and/or in patients taking concomitant CYP3A4 inhibitors or CYP2D6 inhibitors for more than 14 days.

Adjustments based on CYP2D6 metabolism or concomitant medications

○ 720 mg once every 2 months ⊖ Avoid use

Factors		ABILIFY ASIMTUFII adjusted dose
CYP2D6 poor metabolizers	Known CYP2D6 poor metabolizers	○
	Known CYP2D6 poor metabolizers taking concomitant CYP3A4 inhibitors	⊖
Patients taking ABILIFY ASIMTUFII	Concomitant use of strong CYP2D6 inhibitors	○
	Concomitant use of strong CYP3A4 inhibitors	○
	Concomitant use of strong CYP2D6 **and** CYP3A4 inhibitors	⊖
	Concomitant use of CYP3A4 inducers	⊖

Important Warning and Precaution for Neuroleptic Malignant Syndrome (NMS)
NMS is a potentially fatal symptom complex reported in association with administration of antipsychotic drugs including aripiprazole. Clinical signs of NMS are hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability. Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. Manage NMS with immediate discontinuation of aripiprazole, intensive symptomatic treatment, and monitoring.

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Neuroleptic Malignant Syndrome (NMS): NMS is a potentially fatal symptom complex reported in association with administration of antipsychotic drugs including ABILIFY ASIMTUFII. Clinical signs of NMS are hyperpyrexia, muscle rigidity, altered mental status and evidence of autonomic instability. Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. Manage NMS with immediate discontinuation of ABILIFY ASIMTUFII, intensive symptomatic treatment, and monitoring.

Tardive Dyskinesia (TD): Risk of TD, and the potential to become irreversible, are believed to increase with duration of treatment and total cumulative dose of antipsychotic drugs. TD can develop after a relatively brief treatment period, even at low doses, or after discontinuation of treatment. Prescribing should be consistent with the need to minimize TD. If antipsychotic treatment is withdrawn, TD may remit, partially or completely.

Metabolic Changes: Atypical antipsychotic drugs have caused metabolic changes including:

- **Hyperglycemia/Diabetes Mellitus:** Hyperglycemia, in some cases extreme and associated with ketoacidosis, hyperosmolar coma, or death, has been reported in patients treated with atypical antipsychotics including aripiprazole. Patients with diabetes mellitus should be regularly monitored for worsening of glucose control; those with risk factors for diabetes (e.g., obesity, family history of diabetes), should undergo baseline and periodic fasting blood glucose testing. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia should also undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required continuation of antidiabetic treatment despite discontinuation of the suspect drug.
- **Dyslipidemia:** Undesirable alterations in lipids have been observed in patients treated with atypical antipsychotics.
- **Weight Gain:** Weight gain has been observed with atypical antipsychotic use. Clinical monitoring of weight is recommended.

Pathological Gambling and Other Compulsive Behaviors: Intense urges, particularly for gambling, and the inability to control these urges have been reported while taking aripiprazole. Other compulsive urges have been reported less frequently. Prescribers should ask patients or their caregivers about the development of new or intense compulsive urges. Consider dose reduction or stopping aripiprazole if such urges develop.

Orthostatic Hypotension or Syncope: ABILIFY ASIMTUFII may cause orthostatic hypotension and should be used with caution in patients with known cardiovascular disease, cerebrovascular disease, or conditions which would predispose them to hypotension. Monitoring of orthostatic vital signs should be considered in patients who are vulnerable to hypotension.

Falls: Antipsychotics may cause somnolence, postural hypotension, motor and sensory instability, which may lead to falls causing fractures or other injuries. For patients with diseases, conditions, or medications that could exacerbate these effects, complete fall risk assessments when initiating treatment and recurrently during therapy.

(Continued on next page)

Please see **FULL PRESCRIBING INFORMATION**, including **BOXED WARNING**.

IMPORTANT SAFETY INFORMATION for ABILIFY ASIMTUFII® (aripiprazole) (cont'd)

Leukopenia, Neutropenia, and Agranulocytosis: Leukopenia, neutropenia, and agranulocytosis have been reported with antipsychotics. Monitor complete blood count in patients with pre-existing low white blood cell count (WBC)/absolute neutrophil count or history of drug-induced leukopenia/neutropenia. Discontinue ABILIFY ASIMTUFII at the first sign of a clinically significant decline in WBC and in severely neutropenic patients.

Seizures: ABILIFY ASIMTUFII should be used with caution in patients with a history of seizures or with conditions that lower the seizure threshold.

Potential for Cognitive and Motor Impairment: ABILIFY ASIMTUFII may impair judgment, thinking, or motor skills. Patients should be cautioned about performing activities that require mental alertness such as operating hazardous machinery or operating a motor vehicle, until they are reasonably certain that therapy with ABILIFY ASIMTUFII does not affect them adversely.

Body Temperature Regulation: Use ABILIFY ASIMTUFII with caution in patients who may experience conditions that increase body temperature (e.g., strenuous exercise, extreme heat, dehydration, or concomitant use with anticholinergics).

Dysphagia: Esophageal dysmotility and aspiration have been associated with aripiprazole. Use caution in patients at risk for aspiration.

Alcohol: Advise patients to avoid alcohol while taking ABILIFY ASIMTUFII.

Concomitant Medications: Dosage reductions are recommended in patients who are CYP2D6 poor metabolizers and/or in patients taking concomitant CYP3A4 inhibitors or CYP2D6 inhibitors for greater than 14 days. Avoid concomitant use of CYP3A4 inducers with ABILIFY ASIMTUFII for greater than 14 days. Dosage adjustments are not recommended for patients with concomitant use of CYP3A4 inhibitors, CYP2D6 inhibitors or CYP3A4 inducers for less than 14 days.

Most Commonly Observed Adverse Reactions: The most commonly observed adverse reactions based on a 12-week study of a once monthly injection of aripiprazole in patients with schizophrenia (incidence of ≥5% and at least twice that for placebo) were increased weight, akathisia, injection site pain, and sedation.

Injection Site Reactions: In an open-label study in patients with schizophrenia or bipolar I disorder, the percent of patients reporting any injection site-related adverse reactions was 19% for ABILIFY ASIMTUFII and 9.0% for once monthly aripiprazole injection. In both treatment groups, the majority of the injection site pain events coincided with the first injection and were reported with decreasing frequency upon subsequent injections. Patient-reported rating of pain was similar in both treatment groups at the last injection.

Dystonia: Symptoms of dystonia may occur in susceptible individuals during the first days of treatment and at low doses.

Pregnancy: Neonates exposed to antipsychotic drugs, including ABILIFY ASIMTUFII, during the third trimester of pregnancy are at risk for extrapyramidal and/or withdrawal symptoms. There are risks to the mother associated with untreated schizophrenia or bipolar I disorder and with exposure to antipsychotics, including ABILIFY ASIMTUFII, during pregnancy.

Lactation: Aripiprazole is present in human breast milk. Monitor the breastfed infant for dehydration and lack of appropriate weight gain. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ABILIFY ASIMTUFII and any potential adverse effects on the breastfed infant from ABILIFY ASIMTUFII or from the underlying maternal condition.

To report SUSPECTED ADVERSE REACTIONS, contact Otsuka America Pharmaceutical, Inc. at 1-800-438-9927 or FDA at 1-800-FDA-1088 (www.fda.gov/medwatch).

Please see accompanying **FULL PRESCRIBING INFORMATION**, including **BOXED WARNING**.

1. National Council for Mental Wellbeing. Guide to long-acting medications for clinicians and organizations. December 2021. Accessed July 2024. https://www.thenationalcouncil.org/resources/guide-to-long-acting-medications/ **2.** Sajatovic M, Ross R, Legacy SN, et al. Initiating/maintaining long-acting injectable antipsychotics in schizophrenia/schizoaffective or bipolar disorder—expert consensus survey part 2. *Neuropsychiatr Dis Treat*. 2018;14:1475-1492. doi:10.2147/NDT.S167485 **3.** Elwyn G, Dehlendorf C, Epstein RM, Marrin K, White J, Frosch DL. Shared decision making and motivational interviewing: achieving patient-centered care across the spectrum of health care problems. *Ann Fam Med*. 2014;12:270-275. **4.** Ennis-O'Connor M. Shared decision making: putting the patient at the center of medical care. Patient Empowerment Network. March 2016. Accessed February 2024. https://powerfulpatients.org/2016/03/27/shared-decision-making-putting-the-patient-at-the-center-of-medical-care/ **5.** Fiorillo A, Barlati S, Bellomo A, Corrivetti G, Nicolo G, Sampogna G, et al. The role of shared decision-making in improving adherence to pharmacological treatments in patients with schizophrenia: a clinical review. *Ann Gen Psychiatry*. 2020;19:43.

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