**INDICATIONS**

ABILIFY MAINTENA is an atypical antipsychotic indicated for:
- Treatment of schizophrenia in adults
- Maintenance monotherapy treatment of bipolar I disorder in adults

**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 MAINTENA is not approved for the treatment of patients with dementia-related psychosis.

Please see IMPORTANT SAFETY INFORMATION on pages 7-9.
AS YOU MAY KNOW...

Current guidelines remind us that periodic reevaluation of a patient’s treatment plan is a part of good clinical practice.5-8

In addition, shared decision-making with patients may play a role in their consideration of treatment options such as an LAI.9-13

Open-ended questions have been shown to help clinicians engage patients in discussions.13

The questions provided in this brochure have been designed not as medical guidance but as examples of this open-ended style.

Determining patients’ attitudes toward their treatment formulations:

• How is your treatment formulation working for you?
• What can I do to help with your treatment?

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

Please see IMPORTANT SAFETY INFORMATION on pages 7-9.
DID YOU KNOW?

• Some psychiatrists may assume that certain patients would choose not to receive LAIs

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Discussing the importance of taking their oral or LAI medication:

• What was it like the last time you stopped taking your medication?

• What do you think would happen if you didn’t receive your medication?

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Important Warning and Precaution Regarding 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.

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Please see IMPORTANT SAFETY INFORMATION on pages 7-9.
LET YOUR PATIENTS KNOW...

- ABILIFY MAINTENA® (aripiprazole) can be used as an alternative to a daily antipsychotic
- Establish tolerability with oral aripiprazole prior to initiating treatment with ABILIFY MAINTENA. Allow up to 2 weeks to fully assess tolerability
- Along with the first injection, treatment with oral aripiprazole or current oral antipsychotic should be continued for 14 days. Only for administration by a healthcare professional. Dosage adjustments are required for missed doses

Considering how a patient would feel about receiving a once-monthly* medication:

- Would it help if you didn’t have to take your antipsychotic every day*?
  - What are your thoughts on receiving your medication once a month?
  - How do you feel about receiving a month’s worth of medicine with one dose?

*Some long-acting formulations require overlapping dosing of oral antipsychotic treatment at initiation.4

Important Warning and Precaution Regarding Neuroleptic Malignant Syndrome (NMS):
NMS is a potentially fatal symptom complex reported in association with administration of antipsychotic drugs including ABILIFY MAINTENA. 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 MAINTENA, intensive symptomatic treatment, and monitoring.

Please see IMPORTANT SAFETY INFORMATION on pages 7-9.
Introducing/Reintroducing an LAI as an alternative to a daily antipsychotic

WHAT IS YOUR EXPERIENCE?
Do you feel that patients who initially reject an LAI may become more receptive to this treatment option if the topic is periodically reintroduced?\(^{15}\)

Introducing/Reintroducing LAIs:

- Have you given more thought to receiving your antipsychotic medicine as a once-monthly* injection?
  - Since the last time we spoke, what thought have you given to receiving this medicine each month with one injection?
  - How do you feel about starting a trial of the once-monthly dosing we talked about?

*Some long-acting formulations require overlapping dosing of oral antipsychotic treatment at initiation.\(^{4}\)

Important Warning and Precaution Regarding 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.

Please see IMPORTANT SAFETY INFORMATION on pages 7-9.
Important Warning and Precaution Regarding Injection Site Reactions:
In a short-term, clinical trial with ABILIFY MAINTENA in patients with schizophrenia treated with gluteal administered ABILIFY MAINTENA, the percent of patients reporting any injection site-related adverse reaction was 5.4%, and 0.6% for placebo. In an open label study of ABILIFY MAINTENA administered in the deltoid or gluteal muscle, injection site pain was observed at approximately equal rates.

Please see Important Safety Information on pages 7-9.
INDICATIONS

ABILIFY MAINTENA 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 MAINTENA is not approved for the treatment of patients with dementia-related psychosis.

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

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.

Neuroleptic Malignant Syndrome (NMS): NMS is a potentially fatal symptom complex reported in association with administration of antipsychotic drugs including ABILIFY MAINTENA. 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 MAINTENA, 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.

(Continued on next page.)

Please see FULL PRESCRIBING INFORMATION, including BOXED WARNING.
• Hyperglycemia/Diabetes Mellitus (continued): 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 anti-diabetic 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: ABILIFY MAINTENA 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.

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.

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 MAINTENA at the first sign of a clinically significant decline in WBC and in severely neutropenic patients.

Seizures: ABILIFY MAINTENA 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 MAINTENA may impair judgment, thinking, or motor skills. Instruct patients to avoid operating hazardous machinery, including automobiles, until they are certain ABILIFY MAINTENA does not affect them adversely.

(Continued on next page.)

Please see FULL PRESCRIBING INFORMATION, including BOXED WARNING.
Body Temperature Regulation: Use ABILIFY MAINTENA 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 ABILIFY MAINTENA. Use caution in patients at risk for aspiration pneumonia.

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

Concomitant Medication: Dosage adjustments are recommended in patients who are CYP2D6 poor metabolizers and in patients taking concomitant CYP3A4 inhibitors or CYP2D6 inhibitors for greater than 14 days. Avoid concomitant use of CYP3A4 inducers with ABILIFY MAINTENA 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 with ABILIFY MAINTENA in patients with schizophrenia (incidence ≥5% and at least twice that for placebo) were increased weight, akathisia, injection site pain, and sedation.

Injection Site Reactions: In a short-term, clinical trial with ABILIFY MAINTENA in patients with schizophrenia treated with gluteal administered ABILIFY MAINTENA, the percent of patients reporting any injection site-related adverse reaction was 5.4%, and 0.6% for placebo. In an open label study of ABILIFY MAINTENA administered in the deltoid or gluteal muscle, injection site pain was observed at approximately equal rates.

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 MAINTENA, during the third trimester of pregnancy are at risk for extrapyramidal and/or withdrawal symptoms. Consider the benefits and risks of ABILIFY MAINTENA and possible risks to the fetus when prescribing ABILIFY MAINTENA to a pregnant woman. Advise pregnant women of potential fetal risk.

Lactation: Aripiprazole is present in human breast milk. A decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother and any potential risks to the infant.

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 FULL PRESCRIBING INFORMATION, including BOXED WARNING.
Pivotal studies for ABILIFY MAINTENA® (aripiprazole)

12-WEEK SCHIZOPHRENIA STUDY\textsuperscript{1,16}

- A randomized, double-blind, placebo-controlled clinical study of 340 acutely relapsed adult patients with schizophrenia to determine the efficacy and safety of ABILIFY MAINTENA 400 mg (n=168) vs placebo (n=172). All patients had a diagnosis of schizophrenia for ≥1 year at study entry.
- In this study, ABILIFY MAINTENA showed significant results in PANSS Total Score vs placebo (at Week 1: $P<0.001$; at Week 2 and all subsequent time points, including primary efficacy endpoint at Week 10: $P<0.0001$).

52-WEEK, MULTIPHASE SCHIZOPHRENIA STUDY\textsuperscript{2}

- Open-label phase (Phase 2), patients with a diagnosis of schizophrenia ≥3 years were stabilized on oral aripiprazole 10 mg to 30 mg/day.
- Single-blind phase (Phase 3), patients were converted to and stabilized on ABILIFY MAINTENA 400 mg (patients also continued on oral aripiprazole 10 mg to 20 mg for the first 14 days following the initial ABILIFY MAINTENA dose).
- Double-blind, placebo-controlled phase (Phase 4), patients were randomized to either intramuscular (IM) ABILIFY MAINTENA (n=269) or IM placebo (n=134).
- In this study, ABILIFY MAINTENA significantly delayed time to relapse vs placebo ($P<0.0001$). ABILIFY MAINTENA showed significant difference in PANSS Total Score vs placebo starting at Week 2 in double-blind Phase 4 and at all subsequent time points (at Week 2: $P<0.05$; at Week 4: $P<0.001$; at Weeks 6 through 52: $P<0.0001$).

52-WEEK, MULTIPHASE BIPOLAR I DISORDER STUDY\textsuperscript{3}

- Open-label phase (Phase 2), patients were stabilized on oral aripiprazole 15 mg to 30 mg/day.
- Single-blind phase (Phase 3), patients were converted to and stabilized on ABILIFY MAINTENA 400 mg (patients also continued on oral aripiprazole 10 mg to 20 mg for the first 14 days following the initial ABILIFY MAINTENA dose).
- Double-blind, placebo-controlled phase (Phase 4), patients were randomized to either IM ABILIFY MAINTENA (n=133) or IM placebo (n=133).
- In this study, ABILIFY MAINTENA significantly delayed time to recurrence of any mood episode vs placebo ($P<0.0001$). ABILIFY MAINTENA significantly delayed time to recurrence for a manic and mixed episode. No substantial difference in the time to a depressive episode.

PANSS=Positive and Negative Syndrome Scale.

Please see IMPORTANT SAFETY INFORMATION on pages 7-9.
Clinical safety profile
for ABILIFY MAINTENA® (aripiprazole)

ABILIFY MAINTENA HAS BEEN EVALUATED FOR SAFETY IN MORE THAN 2000 ADULT PATIENTS WITH SCHIZOPHRENIA AND IN MORE THAN 800 ADULT PATIENTS WITH BIPOLAR I DISORDER

The following safety information is derived from a 12-week, double-blind study or an open-label study in schizophrenia.

• Most commonly observed adverse reactions (incidence ≥5% for ABILIFY MAINTENA and at least twice that for placebo) were increased weight, akathisia, injection site pain, and sedation
  —The mean intensity of injection pain reported by patients using a visual analog scale (0=no pain to 100=unbearably painful) approximately 1 hour after injection was 7.1 (SD 14.5) for the first injection and 4.8 (SD 12.4) at the last visit

INJECTION PAIN REPORTED BY PATIENTS WITH SCHIZOPHRENIA

7.1 (14.5) – 1 hour after first injection

4.8 (12.4) at the last visit

• In an open-label study comparing bioavailability of ABILIFY MAINTENA administered in the deltoid or gluteal muscle, injection site pain was observed in both groups at approximately equal rates

SD=standard deviation.


Please see IMPORTANT SAFETY INFORMATION on pages 7-9.
Discussing ABILIFY MAINTENA® (aripiprazole) as an LAI treatment option with appropriate patients

The first and only FDA-approved once-monthly* injectable for both schizophrenia and maintenance monotherapy treatment of bipolar I disorder in adults

*Establish tolerability with oral aripiprazole before initiating therapy. Along with the first injection, patients should take oral aripiprazole or current oral antipsychotic for 14 consecutive days.

Make ABILIFY MAINTENA your choice for an LAI

- For patients who have never taken aripiprazole, establish tolerability with oral aripiprazole prior to initiating treatment with ABILIFY MAINTENA. Due to the half-life of oral aripiprazole, it may take up to 2 weeks to fully assess tolerability.
- Along with the first injection, patients should also receive a prescription for oral aripiprazole (10 mg to 20 mg) or current oral antipsychotic for 14 consecutive days.
- Please specify either the pre-filled, dual chamber syringe or the vial kit when writing either an electronic or a conventional prescription.

Please visit ABILIFYMAINTENAhcp.com for more information.

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