HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use ABILIFY safely and effectively. See full prescribing information for ABILIFY.

ABILIFY® (aripiprazole) Tablets
ABILIFY DISCMELT® (aripiprazole) Orally Disintegrating Tablets
ABILIFY® (aripiprazole) Oral Solution
ABILIFY® (aripiprazole) Injection FOR INTRAMUSCULAR USE ONLY

Initial U.S. Approval: 2002

WARNINGS: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS and SUICIDALITY AND ANTIDEPRESSANT DRUGS

See full prescribing information for complete boxed warning.

- **Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. ABILIFY is not approved for the treatment of patients with dementia-related psychosis. (5.1)**
- **Children, adolescents, and young adults taking antidepressants for major depressive disorder (MDD) and other psychiatric disorders are at increased risk of suicidal thinking and behavior. (5.2)**

----------RECENT MAJOR CHANGES----------

Indications and Usage, Bipolar I Disorder, Adjunctive Therapy (1.2)	02/2011
Dosage and Administration, Bipolar I Disorder, Adjunctive Therapy (2.2)	02/2011
Dosage and Administration, Dosage Adjustment (2.6)	02/2011

----------INDICATIONS AND USAGE----------

ABILIFY is an atypical antipsychotic indicated as oral formulations for the:

Treatment of schizophrenia (1.1)

- Adults: Efficacy was established in four 4-6 week trials and one maintenance trial in patients with schizophrenia (14.1)
- Adolescents (ages 13-17): Efficacy was established in one 6-week trial in patients with schizophrenia (14.1)

Acute treatment of manic or mixed episodes associated with bipolar I disorder as monotherapy and as an adjunct to lithium or valproate (1.2)

- Adults: Efficacy was established in four 3-week monotherapy trials and one 6-week adjunctive trial in patients with manic or mixed episodes (14.2)
- Pediatric Patients (ages 10-17): Efficacy was established in one 4-week monotherapy trial in patients with manic or mixed episodes (14.2)

Maintenance treatment of bipolar I disorder, both as monotherapy and as an adjunct to lithium or valproate (1.2)

- Adults: Efficacy was established in one maintenance monotherapy trial and in one maintenance adjunctive trial (14.2)
- Adjunctive treatment of major depressive disorder (MDD) (1.3)
- Adults: Efficacy was established in two 6-week trials in patients with MDD who had an inadequate response to antidepressant therapy during the current episode (14.3)

Treatment of irritability associated with autistic disorder (1.4)

- Pediatric Patients (ages 6-17 years): Efficacy was established in two 8-week trials in patients with autistic disorder (14.4)

as an injection for the:

Acute treatment of agitation associated with schizophrenia or bipolar I disorder (1.5)

- Adults: Efficacy was established in three 24-hour trials in agitated patients with schizophrenia or manic/mixed episodes of bipolar I disorder (14.5)

----------DOSAGE AND ADMINISTRATION----------

	Initial Dose	Recommended Dose	Maximum Dose
Schizophrenia – adults (2.1)	10-15 mg /day	10-15 mg /day	30 mg /day
Schizophrenia – adolescents (2.1)	2 mg /day	10 mg /day	30 mg /day
Bipolar mania – adults: monotherapy (2.2)	15 mg /day	15 mg /day	30 mg /day
Bipolar mania – adults: adjunct to lithium or valproate (2.2)	10-15 mg /day	15 mg /day	30 mg /day
Bipolar mania – pediatric patients: monotherapy or as an adjunct to lithium or valproate (2.2)	2 mg /day	10 mg /day	30 mg /day
As an adjunct to antidepressants for the treatment of major depressive disorder – adults (2.3)	2-5 mg /day	5-10 mg /day	15 mg /day
Irritability associated with autistic disorder – pediatric patients (2.4)	2 mg/day	5-10 mg/day	15 mg/day
Agitation associated with schizophrenia or bipolar mania – adults (2.5)	9.75 mg /1.3 mL injected IM		30 mg/day injected IM

- Oral formulations: Administer once daily without regard to meals (2)
- IM injection: Wait at least 2 hours between doses. Maximum daily dose 30 mg (2.5)

----------DOSAGE FORMS AND STRENGTHS----------

- Tablets: 2 mg, 5 mg, 10 mg, 15 mg, 20 mg, and 30 mg (3)
- Orally Disintegrating Tablets: 10 mg and 15 mg (3)
- Oral Solution: 1 mg/mL (3)
- Injection: 9.75 mg/1.3 mL single-dose vial (3)

----------CONTRAINDICATIONS----------

Known hypersensitivity to ABILIFY (4)

----------WARNINGS AND PRECAUTIONS----------

- *Elderly Patients with Dementia-Related Psychosis:* Increased incidence of cerebrovascular adverse events (eg, stroke, transient ischemic attack, including fatalities) (5.1)
- *Suicidality and Antidepressants:* Increased risk of suicidality in children, adolescents, and young adults with major depressive disorder (5.2)
- *Neuroleptic Malignant Syndrome:* Manage with immediate discontinuation and close monitoring (5.3)
- *Tardive Dyskinesia:* Discontinue if clinically appropriate (5.4)
- *Hyperglycemia and Diabetes Mellitus:* Monitor glucose regularly in patients with and at risk for diabetes (5.5)
- *Orthostatic Hypotension:* Use with caution in patients with known cardiovascular or cerebrovascular disease (5.6)
- *Leukopenia, Neutropenia, and Agranulocytosis:* have been reported with antipsychotics including ABILIFY. Patients with a history of a clinically significant low white blood cell count (WBC) or a drug-induced leukopenia/neutropenia should have their complete blood count (CBC) monitored frequently during the first few months of therapy and discontinuation of ABILIFY should be considered at the first sign of a clinically significant decline in WBC in the absence of other causative factors (5.7)
- *Seizures/Convulsions:* Use cautiously in patients with a history of seizures or with conditions that lower the seizure threshold (5.8)
- *Potential for Cognitive and Motor Impairment:* Use caution when operating machinery (5.9)
- *Suicide:* The possibility of a suicide attempt is inherent in schizophrenia and bipolar disorder. Closely supervise high-risk patients (5.11)

----------ADVERSE REACTIONS----------

Commonly observed adverse reactions (incidence ≥5% and at least twice that for placebo) were (6.2):

- Adult patients with schizophrenia: akathisia
- Pediatric patients (13 to 17 years) with schizophrenia: extrapyramidal disorder, somnolence, and tremor
- Adult patients (monotherapy) with bipolar mania: akathisia, sedation, restlessness, tremor, and extrapyramidal disorder
- Adult patients (adjunctive therapy with lithium or valproate) with bipolar mania: akathisia, insomnia, and extrapyramidal disorder
- Pediatric patients (10 to 17 years) with bipolar mania: somnolence, extrapyramidal disorder, fatigue, nausea, akathisia, blurred vision, salivary hypersecretion, and dizziness
- Adult patients with major depressive disorder (adjunctive treatment to antidepressant therapy): akathisia, restlessness, insomnia, constipation, fatigue, and blurred vision
- Pediatric patients (6 to 17 years) with autistic disorder: sedation, fatigue, vomiting, somnolence, tremor, pyrexia, drooling, decreased appetite, salivary hypersecretion, extrapyramidal disorder, and lethargy
- Adult patients with agitation associated with schizophrenia or bipolar mania: nausea

To report SUSPECTED ADVERSE REACTIONS, contact Bristol-Myers Squibb at 1-800-721-5072 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------DRUG INTERACTIONS----------

- *Strong CYP3A4 (eg, ketoconazole) or CYP2D6 (eg, fluoxetine) inhibitors will increase* ABILIFY drug concentrations; reduce ABILIFY dose to one-half of the usual dose when used concomitantly (2.6, 7.1), except when used as adjunctive treatment with antidepressants (2.6). If a strong CYP3A4 inhibitor and strong CYP2D6 inhibitor are co-administered or a known CYP2D6 poor metabolizer is receiving a concomitant strong CYP3A4 inhibitor, the ABILIFY dose should be reduced to one-quarter (25%) of the usual dose (2.6, 12.3).
- *CYP3A4 inducers (eg, carbamazepine) will decrease* ABILIFY drug concentrations; double ABILIFY dose when used concomitantly (2.6, 7.1)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide

Revised: 02/2011

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

WARNINGS: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS and SUICIDALITY AND ANTIDEPRESSANT DRUGS

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. Analyses of seventeen placebo-controlled trials (modal duration of 10 weeks), largely in patients taking atypical antipsychotic drugs, revealed a risk of death in drug-treated patients of between 1.6 to 1.7 times the risk of death in placebo-treated patients. Over the course of a typical 10-week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (eg, heart failure, sudden death) or infectious (eg, pneumonia) in nature. Observational studies suggest that, similar to atypical antipsychotic drugs, treatment with conventional antipsychotic drugs may increase mortality. The extent to which the findings of increased mortality in observational studies may be attributed to the antipsychotic drug as opposed to some characteristic(s) of the patients is not clear. ABILIFY (aripiprazole) is not approved for the treatment of patients with dementia-related psychosis *[see WARNINGS AND PRECAUTIONS (5.1)]*.

Antidepressants increased the risk compared to placebo of suicidal thinking and behavior (suicidality) in children, adolescents, and young adults in short-term studies of major depressive disorder (MDD) and other psychiatric disorders. Anyone considering the use of adjunctive ABILIFY or any other antidepressant in a child, adolescent, or young adult must balance this risk with the clinical need. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; there was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older. Depression and certain other psychiatric disorders are themselves associated with increases in the risk of suicide. Patients of all ages who are started on antidepressant therapy should be monitored appropriately and observed closely for clinical worsening, suicidality, or unusual changes in behavior. Families and caregivers should be advised of the need for close observation and communication with the prescriber. ABILIFY is not approved for use in pediatric patients with depression *[see WARNINGS AND PRECAUTIONS (5.2)]*.

1 INDICATIONS AND USAGE

1.1 Schizophrenia

ABILIFY is indicated for the treatment of schizophrenia. The efficacy of ABILIFY was established in four 4-6 week trials in adults and one 6-week trial in adolescents (13 to 17 years). Maintenance efficacy was demonstrated in one trial in adults and can be extrapolated to adolescents *[see CLINICAL STUDIES (14.1)]*.

1.2 Bipolar I Disorder

Acute Treatment of Manic and Mixed Episodes

ABILIFY is indicated for the acute treatment of manic and mixed episodes associated with bipolar I disorder, both as monotherapy and as an adjunct to lithium or valproate. Efficacy as monotherapy was established in four 3-week monotherapy trials in adults and one 4-week monotherapy trial in pediatric patients (10 to 17 years). Efficacy as adjunctive therapy was established in one 6-week adjunctive trial in adults *[see CLINICAL STUDIES (14.2)]*.

Maintenance Treatment of Bipolar I Disorder

ABILIFY is indicated for the maintenance treatment of bipolar I disorder, both as monotherapy and as an adjunct to either lithium or valproate. Maintenance efficacy was demonstrated in one monotherapy maintenance trial and in one adjunctive maintenance trial in adults *[see CLINICAL STUDIES (14.2)]*.

1.3 Adjunctive Treatment of Major Depressive Disorder

ABILIFY is indicated for use as an adjunctive therapy to antidepressants for the treatment of major depressive disorder (MDD). Efficacy was established in two 6-week trials in adults with MDD who had an inadequate response to antidepressant therapy during the current episode *[see CLINICAL STUDIES (14.3)]*.

1.4 Irritability Associated with Autistic Disorder

ABILIFY is indicated for the treatment of irritability associated with autistic disorder. Efficacy was established in two 8-week trials in pediatric patients (aged 6 to 17 years) with irritability associated with autistic disorder (including symptoms of aggression towards others, deliberate self-injuriousness, temper tantrums, and quickly changing moods) *[see CLINICAL STUDIES (14.4)]*.

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