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----------

Boxed Warning, Suicidality and Antidepressant Drugs	11/2007
Boxed Warning, Increased Mortality in Elderly Patients with Dementia-Related Psychosis	xx/2008
Indications and Usage,	
Adolescent (13 to 17 years) Schizophrenia (1.1)	05/2008
Adjunctive Therapy (Lithium or Valproate) in Adult and Pediatric (10 to 17 years) Patients with Bipolar Mania (1.2)	05/2008
Pediatric (10 to 17 years) Bipolar Mania (1.2)	05/2008
Adjunctive Treatment in Adults with MDD (1.3)	11/2007
Dosage and Administration,	
Adolescent Schizophrenia (2.1)	05/2008
15 mg starting dose in Bipolar Mania (2.2)	05/2008
Adjunctive Therapy (Lithium or Valproate) in Adult and Pediatric Patients with Bipolar Mania (2.2)	05/2008
Pediatric Bipolar Mania (2.2)	05/2008
Adjunctive Treatment in Adults with MDD (2.3)	11/2007
Warnings and Precautions, Clinical Worsening of Depression and Suicide Risk (5.2)	11/2007

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

ABILIFY is an atypical antipsychotic indicated as oral formulations for:

- Treatment of Schizophrenia in adults and adolescents aged 13 to 17 years (1.1)
- Treatment of manic or mixed episodes associated with Bipolar I Disorder as monotherapy or adjunctive to lithium or valproate in adults and pediatric patients aged 10 to 17 years (1.2)
- Adjunctive treatment of Major Depressive Disorder in adults (1.3)

as an injection for:

- Treatment of adults with agitation associated with Schizophrenia or Bipolar I Disorder, manic or mixed episodes (1.4)

----------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 or as an adjunct to lithium or valproate (2.2)	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 (2.3)	2-5 mg /day	5-10 mg /day	15 mg /day
Agitation associated with Schizophrenia or Bipolar Mania – adults (2.4)	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 (2.4)

----------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)
- *Seizures/Convulsions:* Use cautiously in patients with a history of seizures or with conditions that lower the seizure threshold (5.7)
- *Potential for Cognitive and Motor Impairment:* Use caution when operating machinery (5.8)
- *Suicide:* The possibility of a suicide attempt is inherent in Schizophrenia and Bipolar Disorder. Closely supervise high-risk patients (5.10)

----------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
- 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 by one-half when used concomitantly (2.5, 7.1), except when used as adjunctive treatment with antidepressants (2.5)
- *CYP3A4 inducers (eg, carbamazepine) will decrease* ABILIFY drug concentrations; double ABILIFY dose when used concomitantly (2.5, 7.1)

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide

Revised: XX/2008

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 acute and maintenance treatment of Schizophrenia in adults and in adolescents 13 to 17 years of age *[see CLINICAL STUDIES (14.1)]*.

1.2 Bipolar Disorder

Monotherapy

ABILIFY is indicated for acute and maintenance treatment of manic and mixed episodes associated with Bipolar I Disorder with or without psychotic features in adults and in pediatric patients 10 to 17 years of age *[see CLINICAL STUDIES (14.2)]*.

Adjunctive Therapy

ABILIFY is indicated as an adjunctive therapy to either lithium or valproate for the acute treatment of manic and mixed episodes associated with Bipolar I Disorder with or without psychotic features in adults and in pediatric patients 10 to 17 years of age *[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 acute treatment of Major Depressive Disorder in adults *[see CLINICAL STUDIES (14.3)]*.

1.4 Agitation Associated with Schizophrenia or Bipolar Mania

ABILIFY Injection is indicated for the acute treatment of agitation associated with Schizophrenia or Bipolar Disorder, manic or mixed in adults. "Psychomotor agitation" is defined in DSM-IV as "excessive motor activity associated with a feeling of inner tension". Patients experiencing agitation often manifest behaviors that interfere with their diagnosis and care (eg, threatening behaviors, escalating or urgently distressing behavior, or self-exhausting behavior), leading clinicians to the use of intramuscular antipsychotic medications to achieve immediate control of the agitation *[see CLINICAL STUDIES (14.4)]*.

2 DOSAGE AND ADMINISTRATION

2.1 Schizophrenia

Usual Dose for Acute Treatment

Adults

The recommended starting and target dose for ABILIFY is 10 mg/day or 15 mg/day administered on a once-a-day schedule without regard to meals. ABILIFY has been systematically evaluated and shown to be effective in a dose range of 10 mg/day to 30 mg/day, when administered as the tablet formulation; however, doses higher than 10 mg/day or 15 mg/day were not more effective than 10 mg/day or 15 mg/day. Dosage increases should not be made before 2 weeks, the time needed to achieve steady-state *[see CLINICAL STUDIES (14.1)]*.

Adolescents

The recommended target dose of ABILIFY is 10 mg/day. Aripiprazole was studied in pediatric patients 13 to 17 years of age with Schizophrenia at daily doses of 10 mg and 30 mg. The starting daily dose of the tablet formulation in these patients was 2 mg, which was titrated to 5 mg after 2 days and to the target dose of 10 mg after 2 additional days. Subsequent dose increases should be administered in 5 mg increments. The 30 mg/day dose was not shown to be more efficacious than the 10 mg/day dose. ABILIFY can be administered without regard to meals *[see CLINICAL STUDIES (14.1)]*.

Maintenance Therapy

Adults

While there is no body of evidence available to answer the question of how long a patient treated with aripiprazole should remain on it, systematic evaluation of patients with Schizophrenia who had been symptomatically stable on other antipsychotic medications for periods of 3 months or longer, were discontinued from those medications, and were then administered ABILIFY 15 mg/day and observed for relapse during a period of up to 26 weeks, has demonstrated a benefit of such maintenance treatment *[see CLINICAL STUDIES (14.1)]*. Patients should be periodically reassessed to determine the need for maintenance treatment.

DOCKET ALARM

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