

CONTACT: David M. Rosen
Bristol-Myers Squibb
Phone: 609-252-5675
Pager: 866-308-4484
david.m.rosen@bms.com

Debra Kaufmann
Otsuka America Pharmaceutical, Inc.
Phone: 240-683-3568
debrak@otsuka.com

Hideki Shirai
Otsuka Pharmaceutical Co., Ltd.
Phone: +81-3-3292-0021
siraih@otsuka.jp

ABILIFY[®] (aripiprazole) GRANTED APPROVAL FOR NEW INDICATION

Efficacy Was Maintained With ABILIFY in Patients with Bipolar I Disorder With a Recent Manic or Mixed Episode Who Had Been Stabilized and Then Maintained For at Least Six Weeks

PRINCETON, N.J., AND TOKYO, JAPAN, March 7, 2005 – Bristol-Myers Squibb Company (NYSE: BMY) and Otsuka Pharmaceutical Co., Ltd. today announced that the U.S. Food and Drug Administration (FDA) approved ABILIFY[®] (aripiprazole) Tablets and Oral Solution for maintaining efficacy in patients with Bipolar I Disorder with a recent manic or mixed episode who had been stabilized and then maintained for at least six weeks. The FDA approved ABILIFY for the treatment of acute bipolar mania, including manic and mixed episodes associated with bipolar disorder, on September 29, 2004.

Clinical data demonstrated that patients who had been stabilized on ABILIFY for at least six weeks experienced a significant delay in time to relapse, the primary outcome measure for this study, as compared with those randomized to placebo.ⁱ The majority of these relapses were due to manic rather than depressive symptoms. There is insufficient data to know whether ABILIFY is effective in delaying the time to occurrence of depression in patients with Bipolar I Disorder. Physicians who elect to use ABILIFY for extended periods, that is, longer than six weeks, should periodically re-evaluate the long-term usefulness of the drug for the individual patient.

“This approval of ABILIFY is important news for patients who suffer from Bipolar I Disorder with manic and mixed episodes, as relapse is unfortunately, very common,” said John Zajecka, M.D., Director, Treatment Research Center, and Associate Professor of Psychiatry, Rush

University Medical Center. “As a physician, it is very encouraging to know that patients can benefit from ABILIFY® (aripiprazole) throughout the different phases of their treatment.”

The latest FDA approval is based on the positive results of a randomized, double-blind, multicenter, placebo-controlled trial designed to compare the maintenance of efficacy of ABILIFY versus placebo, measured by time to relapse. In this study, patients who had recently experienced a manic or mixed episode were first stabilized with ABILIFY for at least six consecutive weeks. After meeting the stabilization criteria [Young Mania Rating Scale Total Score (Y-MRS) less than or equal to 10 and Montgomery-Asberg Depression Rating Scale (MADRS) less than or equal to 13 during four consecutive visits over a minimum of six weeks], 161 patients were given ABILIFY or placebo in the double-blind, randomization phase.ⁱⁱ

The primary endpoint was time to relapse of manic and depressive symptoms. Of those patients who experienced a relapse, patients treated with ABILIFY relapsed significantly later than placebo-treated patients (p-value equals 0.020)ⁱⁱⁱ. In addition, the total number of relapses was significantly fewer in patients treated with ABILIFY than with placebo^{iv} (25 percent versus 43 percent, respectively; p-value equals 0.013)^v. The majority of these relapses were due to manic rather than depressive symptoms. There is insufficient data to know whether ABILIFY is effective in delaying the time to occurrence of depression in patients with Bipolar I Disorder. The adverse events reported during this trial were generally consistent with those reported in other long-term placebo-controlled trials of ABILIFY.^{vi}

“Bristol-Myers Squibb is pleased that ABILIFY received this important new treatment indication, now providing one medication that can help physicians and patients manage the illness,” said Anthony Hooper, president, U.S. Pharmaceuticals, Bristol-Myers Squibb. “Our company is committed to providing important new treatment options for the millions of people suffering from mental illness and addressing the needs of their healthcare providers and families.”

“We are extremely pleased that ABILIFY, the first and only available dopamine partial agonist, has reached another important milestone in the treatment of mental illness,” said Tatsuo Higuchi, president and representative director, Otsuka Pharmaceutical Co., Ltd. “With this new indication, patients who have had success with ABILIFY during a manic or mixed phase can safely and effectively address their continuing therapy needs.”

About ABILIFY[®] (aripiprazole)

ABILIFY[®] (aripiprazole) is indicated for the treatment of schizophrenia, acute manic and mixed episodes associated with bipolar disorder, and now for maintaining efficacy in patients with Bipolar I Disorder with a recent manic or mixed episode who had been stabilized and then maintained for at least six weeks. Since its initial approval in 2002, over 3.7 million prescriptions have been written in the United States.^{vii}

ABILIFY is available by prescription only. In addition to administration as a once-daily oral tablet, ABILIFY was recently FDA-approved in an oral solution formulation. Now available in U.S. pharmacies, ABILIFY Oral Solution is an important new treatment option for adult patients who are unable to or have difficulty swallowing tablets, and provides flexibility in addressing individual patient needs. Patients should talk to their healthcare provider for more information. To learn more about ABILIFY and for full product information, please visit www.ABILIFY.com.

Important Safety Information

As with all antipsychotic medications, including ABILIFY, a rare condition referred to as neuroleptic malignant syndrome (NMS) has been reported. As with all antipsychotic medications, prescribing should be consistent with the need to minimize the risk of tardive dyskinesia (TD).

Cerebrovascular adverse events (e.g., stroke, transient ischemic attack), including fatalities, have been reported at an increased incidence in clinical trials of elderly patients with dementia-related psychosis treated with ABILIFY, including a significant dose response relationship in a fixed dose trial. ABILIFY is not approved for the treatment of patients with dementia-related psychosis.

Hyperglycemia, including some serious cases ranging from ketoacidosis, hyperosmolar coma, or death, has been reported in patients treated with atypical antipsychotics. ABILIFY was not included in epidemiologic studies suggesting this risk; therefore the risk of hyperglycemia with ABILIFY is not known. However, there have been few reports of hyperglycemia in patients treated with ABILIFY. Patients should be appropriately tested before and monitored during treatment.

ABILIFY may be associated with orthostatic hypotension and should be used with caution in patients with known cardiovascular disease, cerebrovascular disease, or conditions which would predispose them to hypotension.

As with other antipsychotic drugs, ABILIFY should be used with caution in patients with a history of seizures or with conditions that lower the seizure threshold. Seizures occurred in 0.3% of bipolar patients treated with ABILIFY in placebo-controlled trials.

Like other antipsychotics, ABILIFY® (aripiprazole) may have the potential to impair judgment, thinking or motor skills. Patients should not drive or operate hazardous machinery until they are certain ABILIFY does not affect them adversely.

Disruption of the body's ability to reduce core body temperature has been attributed to antipsychotics. Appropriate care is advised for patients who may exercise strenuously, be exposed to extreme heat, receive concomitant medications with anticholinergic activity, or be subject to dehydration.

As antipsychotics have been associated with esophageal dysmotility and aspiration, ABILIFY should be used cautiously in patients at risk for aspiration pneumonia.

As the possibility of a suicide attempt is inherent in psychotic illness and bipolar disorder, close supervision of high-risk patients should accompany drug therapy.

Physicians should determine if a patient is pregnant or intends to become pregnant while taking ABILIFY. Patients should be advised not to drink alcohol, or breast-feed while taking ABILIFY.

Both CYP3A4 and CYP2D6 are responsible for ABILIFY metabolism. Agents that induce CYP3A4 (e.g., carbamazepine) could cause an increase in ABILIFY clearance and lower blood levels. Inhibitors of CYP3A4 (e.g., ketoconazole) or CYP2D6 (e.g., quinidine, fluoxetine, or paroxetine) can inhibit ABILIFY elimination and cause increased blood levels.

Commonly observed adverse events reported with ABILIFY in 3-week bipolar mania trials at a $\geq 5\%$ incidence for ABILIFY and at a rate at least twice the rate of placebo include, respectively, akathisia (15% vs 4%), constipation (13% vs 6%), and accidental injury (6% vs 3%).

Treatment-emergent adverse events reported with ABILIFY in short-term trials at an incidence $\geq 10\%$ and greater than placebo, respectively, include headache (31% vs 26%), agitation (25% vs 24%), anxiety (20% vs 17%), insomnia (20% vs 15%), nausea (16% vs 12%), dyspepsia (15% vs 13%), somnolence (12% vs 8%), akathisia (12% vs 5%), lightheadedness (11% vs 8%), vomiting (11% vs 6%), and constipation (11% vs 7%).

The adverse events reported in a 26-week, double-blind schizophrenia trial comparing ABILIFY and placebo were generally consistent with those reported in the short-term, placebo-controlled schizophrenia trials, except for a higher incidence of tremor: 9% for ABILIFY vs 1% for placebo. In addition, in a long-term (52-week), active-controlled study, the incidence of tremor for ABILIFY was 4%.

ABILIFY is taken once daily with or without food.

About Bristol-Myers Squibb and Otsuka Pharmaceutical Co., Ltd.

Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co., Ltd. are collaborative partners in the development and commercialization of aripiprazole in the United States and major European countries.

Aripiprazole was discovered by Otsuka Pharmaceutical Co., Ltd. Founded in 1964, Otsuka Pharmaceutical Co., Ltd. is a healthcare company with the mission statement: “Otsuka - people creating new products for better health worldwide.” Otsuka researches, develops, manufactures and markets innovative products, focusing its core businesses on pharmaceutical products for the treatment of disease and consumer products for the maintenance of everyday health. Otsuka leads a corporate group comprised of 73 companies and approximately 23,000 people around the world. With 39 consolidated subsidiaries employing approximately 17,000 people, Otsuka earned US \$4.4 billion in consolidated annual revenues in fiscal 2003.

Bristol-Myers Squibb is a global pharmaceutical and related health care products company whose mission is to extend and enhance human life.

#

For more information and full prescribing information, visit: www.ABILIFY.com

Visit Bristol-Myers Squibb on the World Wide Web at: <http://www.bms.com>

Visit Otsuka Pharmaceutical Co., Ltd. at: <http://www.otsuka.co.jp>

ⁱ ABILIFY Product Labeling, p. 10.

ⁱⁱ ABILIFY Product Labeling, p. 10.

ⁱⁱⁱ Final study report, p.5.

^{iv} Final study report, p.6.

^v Final study report, p.5.

^{vi} ABILIFY Product Labeling, p. 29.

^{vii} IMS Weekly NPA Plus, Verispan longitudinal database as of February 11, 2005.