



NDA 21-436 / S-028  
NDA 21-713 / S-020  
NDA 21-729 / S-013  
NDA 21-866 / S-014

Otsuka Pharmaceutical Development & Commercialization, Inc.  
Attention: Kusuma Mallikaarjun, Ph.D.  
Senior Director, Regulatory Affairs  
2440 Research Boulevard  
Rockville, MD 20850

Dear Dr. Mallikaarjun:

Please refer to your supplemental new drug applications dated and received on May 5, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for ABILIFY (aripiprazole) Tablets 2 mg, 5 mg, 10 mg, 15 mg, 20 mg, and 30 mg [NDA 21-436], ABILIFY (aripiprazole) Oral Solution 1 mg / mL [NDA 21-713], ABILIFY DISCMELT (aripiprazole) Orally Disintegrating Tablets 10 mg and 15 mg [NDA 21-729], and ABILIFY (aripiprazole) Injection 9.75 mg / 1.3 mL (7.5 mg / mL) [NDA 21-866].

We acknowledge receipt of your submissions dated June 17, 2009, to each of the supplements referenced above.

Reference is made to our letter dated April 5, 2009, notifying you, under Section 505(o)(4) of the FDCA, of new safety information that we believe should be included in the labeling for the entire class of antipsychotic drugs. This information pertains to the risk of leukopenia, neutropenia, and agranulocytosis.

We also refer you to the letter we sent on June 2, 2009, informing you that we determined that a 30-day extension of the discussion period was warranted to allow us to complete our review and reach agreement on the content of the labeling. We also refer to modified labeling language that we sent to you via email on June 9, 2009.

The supplemental new drug applications, as amended, provide for the addition of the subsection PRECAUTIONS/ Leukopenia, Neutropenia and Agranulocytosis to the labeling for ABILIFY (aripiprazole).

We have completed our review of these supplemental applications, as amended. These applications are approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text (text for the package insert).

#### **CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at

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<http://www.fda.gov/oc/datacouncil/spl.html> that is identical to the enclosed labeling (text for the package insert). Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, **“SPL for approved supplements NDA 21-436 / S-028, NDA 21-713 / S-020, NDA 21-729 / S-013, and NDA 21-866 / S-014.”**

In addition, within 21 days of the date of this letter, amend any pending applications for these NDAs with content of labeling in structured product labeling (SPL) format to include the changes approved in these applications.

Failure to make these changes within the specified period of time could make your product misbranded under 21 USC 321(n) and 352(a).

We request that the revised labeling approved today be available on your website within 10 days of receipt of this letter.

### **LETTERS TO HEALTH CARE PROFESSIONALS**

If you issue a letter communicating important information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit a copy of the letter to these NDAs and a copy to the following address:

MEDWATCH  
Food and Drug Administration  
5515 Security Lane  
HFD-001, Suite 5100  
Rockville, MD 20852

### **REPORTING REQUIREMENTS**

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, please contact Doris J. Bates, Ph.D., Safety Regulatory Project Manager, at (301)796-2260.

Sincerely,

*{See appended electronic signature page}*

Thomas P. Laughren, M.D.  
Director  
Division of Psychiatry Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

Enclosure: Package Insert labeling

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**This is a representation of an electronic record that was signed electronically and  
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/s/

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Mitchell Mathis  
7/19/2009 07:53:08 AM  
For Dr. Laughren