



NDA 20272/S-064  
NDA 20588/S-052  
NDA 21444/S-040  
NDA 21346/S-042

## SUPPLEMENT APPROVALS

Ortho McNeil Janssen Pharmaceuticals, Inc.  
Attention: Patricia Treichler, Associate Director  
Regulatory Affairs  
1125 Trenton-Harbourton Road  
P.O. Box 200  
Titusville, NJ 08560-0200

Dear Ms. Treichler:

Please refer to your Supplemental New Drug Applications (sNDA) dated April 28, 2011, received April 29, 2011, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Risperdal (risperidone) tablets, oral solution, Risperdal M-Tab (risperidone) orally disintegrating tablets, and Risperdal Consta (risperidone) long-acting injection.

These "Changes Being Effected" supplemental new drug applications provide for the addition of new adverse drug reactions:

### **6.3 Commonly-Observed Adverse Reactions in Double-Blind, Placebo-Controlled Clinical Trials - Autistic Disorder**

In another study with patients treated for irritability associated with autistic disorder, headache (6%), epistaxis (6%) and pyrexia (6%) were also observed in RISPERDAL®- treated pediatric subjects.

### **6.4 Other Adverse Reactions Observed During the Clinical Trial Evaluation of Risperidone**

Blood and Lymphatic System Disorders: granulocytopenia, neutropenia  
Nervous System Disorders: balance disorder, disturbance in attention, dysarthria, unresponsive to stimuli, depressed level of consciousness, movement disorder, hypersomnia, transient ischemic attack, coordination abnormal, cerebrovascular accident, speech disorder, loss of consciousness, hypoesthesia, tardive dyskinesia, cerebral ischemia, cerebrovascular disorder, neuroleptic malignant syndrome, diabetic coma, head titubation

## **6.9 Postmarketing Experience**

The following adverse reactions have been identified during postapproval use of risperidone; because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency: agranulocytosis, alopecia, anaphylactic reaction, angioedema, atrial fibrillation, blood cholesterol increased, blood triglycerides increased, diabetes mellitus, diabetic ketoacidosis in patients with impaired glucose metabolism, drug withdrawal syndrome neonatal, dysgeusia, hypoglycemia, hypothermia, inappropriate antidiuretic hormone secretion, intestinal obstruction, jaundice, mania, pancreatitis, priapism, QT prolongation, sleep apnea syndrome, thrombocytopenia, urinary retention, and water intoxication.

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

### **CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling with the addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eLIST may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As” at <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

### **REPORTING REQUIREMENTS**

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

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If you have any questions, please email Ann Sohn, Regulatory Project Manager, at [ann.sohn@fda.hhs.gov](mailto:ann.sohn@fda.hhs.gov).

Sincerely,

*{See appended electronic signature page}*

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

ENCLOSURE:  
Content of Labeling

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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THOMAS P LAUGHREN  
06/15/2011