



NDA 20272/S-055/S-058/S-061/S-062  
NDA 20588/S-043/S-046/S-049/S-050  
NDA 21444/S-030/S-033/S-036/S-037

## SUPPLEMENT APPROVALS

Johnson & Johnson Pharmaceutical Research & Development, L.L.C.  
Attention: Patricia K. 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 December 23, 2008 (S-055, S-043, & S-030), November 30, 2009 (S-058, S-046, & S-033), April 12, 2010 (S-061, S-049, & S-036) and May 28, 2010 (S-062, S-050, & S-037) received December 24, 2008, December 1, 2009, April 13, 2010 and May 28, 2010, respectively, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Risperdal (risperidone) tablets (NDA 20272), Risperdal (risperidone) oral solution (NDA 20588), and Risperdal M-Tab (risperidone) oral disintegrating tablets (NDA 21444).

### **NDA 20272/S-055, NDA 20588/S-043, NDA21444/S-030**

These "Prior Approval" supplemental new drug applications propose changes to the Adverse Reactions section to present the adverse drug reactions using Medical Dictionary for Regulatory Activities (MeDRA) terminology instead of World Health Organization Adverse Reactions Terminology (WHOART). See annotated labeling.

Also added is the following revision to the Dosage and Administration, Adolescents section:

There are no controlled data to support the longer term use of RISPERDAL® beyond 8 weeks in adolescents with schizophrenia. The physician who elects to use RISPERDAL® for extended periods in adolescents with schizophrenia should periodically re-evaluate the long-term ~~usefulness~~ risks and benefits of the drug for the individual patient.

There is the following revision to the Priapism section:

### **5.11 Priapism**

~~Rare cases of priapism have been reported. While the relationship of the events to RISPERDAL® use has not been established, other drugs with alpha-adrenergic blocking effects have been reported to induce priapism, and it is possible that RISPERDAL® may~~

~~share this capacity.~~ Priapism has been reported during postmarketing surveillance /see Adverse Reactions (6.9)].<sup>2</sup> Severe priapism may require surgical intervention.

And there are following additions to the Postmarketing Experience section:

### **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, diabetic ketoacidosis in patients with impaired glucose metabolism, inappropriate antidiuretic hormone secretion, hypothermia,<sup>5</sup> intestinal obstruction, jaundice, mania, pancreatitis, priapism,<sup>6</sup> QT prolongation, sleep apnea syndrome,<sup>7</sup> thrombocytopenia, and water intoxication.

### **NDA 20272/S-058, NDA 20588/S-046, NDA 21444/S-033**

The “Changes Being Effected” supplemental new drug applications provide for the addition of urinary retention to the Postmarketing Experience section.

### **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, diabetic ketoacidosis in patients with impaired glucose metabolism, inappropriate antidiuretic hormone secretion, intestinal obstruction, jaundice, mania, pancreatitis, QT prolongation, sleep apnea, thrombocytopenia, urinary retention<sup>1</sup>, and water intoxication.

### **NDA 20272/S-061, NDA 20588/S-049, NDA 21444/S-036**

The “Changes Being Effected” supplemental new drug applications provide for the addition of diabetes mellitus and hypoglycemia to the Postmarketing Experience section.

### **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, diabetes mellitus<sup>i</sup>, diabetic ketoacidosis in patients with impaired glucose metabolism, hypoglycemia<sup>ii</sup>, inappropriate antidiuretic hormone secretion,

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intestinal obstruction, jaundice, mania, pancreatitis, QT prolongation, sleep apnea, thrombocytopenia, urinary retention, and water intoxication.

**NDA 20272/S-062, NDA 20588/S-050, NDA 21444/S-037**

The “Prior Approval” supplemental new drug applications propose changes to the Hyperglycemia and Diabetes and Mellitus subsection within the Warnings and Precautions section.

Hyperglycemia and diabetes mellitus, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, have ~~has~~ been reported in patients treated with antipsychotics including Risperdal.

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, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>, that is identical to the enclosed labeling (text for the package insert and Medication Guide) and include the labeling changes proposed in any pending “Changes Being Effected” (CBE) supplements. 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 via publicly available labeling repositories.

**LETTERS TO HEALTH CARE PROFESSIONALS**

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA, to CDERMedWatchSafetyAlerts@fda.hhs.gov, and to the following address:

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MedWatch  
Food and Drug Administration  
Suite 12B-05  
5600 Fishers Lane  
Rockville, MD 20857

## **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, 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: 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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MITCHELL V Mathis  
08/30/2010  
For Dr. Laughren