DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 21346/S-031/S-035/S-038/S-039 **SUPPLEMENT APPROVALS**

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

Dear Ms. Treichler:

Please refer to your Supplemental New Drug Applications (sNDA) dated December 23, 2008 (S-031), November 19, 2009 (S-035), April 12, 2010 (S-038), and May 28, 2010 9S-039) received December 24, 2008, November 20, 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 Consta (risperidone) long-acting injection.

S-031
The "Prior Approval" supplemental new drug application proposes the addition of adverse drug reactions associated with risperidone that have been reported with oral Risperdal but not identified as ADRs in clinical studies with Risperdal Consta.

Other Adverse Reactions Observed During the Premarketing Evaluation of RISPERDAL® CONSTA® Risperidone

Additional Adverse Reactions Reported with Oral RISPERDAL®2

The following is a list of additional adverse reactions that have been reported during the premarketing evaluation of oral RISPERDAL®, regardless of frequency of occurrence:
Blood and Lymphatic Disorders: granulocytopenia
Cardiac Disorders: atrioventricular block
Ear and Labyrinth Disorders: tinnitus
Eye Disorders: ocular hyperemia, eye discharge, eye rolling, eyelid edema, eye swelling, eyelid margin crusting, dry eye, lacrimation increased, photophobia, glaucoma
Gastrointestinal Disorders: abdominal pain upper, dysphagia, fecaloma, abdominal discomfort, fecal incontinence, lip swelling, cheilitis, aptyalism
General Disorders: thirst, feeling abnormal, gait disturbance, pitting edema, edema, chills, discomfort, generalized edema, drug withdrawal syndrome, peripheral coldness
Immune System Disorders: drug hypersensitivity
Infections and Infestations: tonsillitis, eye infection, cellulitis, otitis media, onychomycosis, acarodermatitis, bronchopneumonia, respiratory tract infection, tracheobronchitis, otitis media chronic
Investigations: body temperature increased, heart rate increased, eosinophil count

increased, white blood cell count decreased, hemoglobin decreased, blood creatine phosphokinase increased, hematocrit decreased, body temperature decreased, blood pressure decreased, transaminases increased
Metabolism and Nutrition Disorders: polydipsia
Musculoskeletal, Connective Tissue, and Bone Disorders: joint swelling, joint stiffness, rhabdomyolysis, torticollis
Nervous System Disorders: hypertonia, balance disorder, dysarthria, unresponsive to stimuli, depressed level of consciousness, movement disorder, hypokinesia, parkinsonian rest tremor, transient ischemic attack, cerebrovascular accident, masked facies, speech disorder, loss of consciousness, muscle contractions involuntary, akinesia, cerebral ischemia, cerebrovascular disorder, neuroleptic malignant syndrome, diabetic coma
Psychiatric Disorders: blunted affect, confusional state, middle insomnia, listless, anorgasmia
Renal and Urinary Disorders: enuresis, dysuria, pollakiuria
Reproductive System and Breast Disorders: vaginal discharge, retrograde ejaculation, ejaculation disorder, ejaculation failure, breast enlargement
Respiratory, Thoracic, and Mediastinal Disorders: epistaxis, wheezing, pneumonia aspiration, dysphonia, productive cough, pulmonary congestion, respiratory tract congestion, rales, respiratory disorder, hyperventilation, nasal edema
Skin and Subcutaneous Tissue Disorders: erythema, skin discoloration, skin lesion, skin disorder, rash erythematous, rash papular, hyperkeratosis, dandruff, seborrheic dermatitis, rash generalised, rash maculopapular
Vascular Disorders: flushing

In addition, "CONSTA®" has been added to the Highlights section under Warnings and Precautions.

----------WARNINGS AND PRECAUTIONS----------
• Cerebrovascular events, including stroke, in elderly patients with dementiarelated psychosis. RISPERDAL® CONSTA® is not approved for use in patients with dementia-related psychosis (5.2)

S-035
The "Changes Being Effected" supplemental new drug application provides for the addition of 7 adverse drug reaction terms not previously identified in clinical trials or post-marketing experience with Risperdal Consta. Six new ADRs (abdominal pain upper, respiratory tract infection, glucose urine present, initial insomnia, ejaculation delayed, pruitus generalized) were identified in study RIS-BMN-3001 and are included in Section 6.3 *Other Adverse Reactions Observed During the Premarketing Evaluation of Risperdal Consta* of the USPI. One new ADR (urinary retention) identified through postmarketing surveillance has been added to Section 6.8 *Postmarketing Experience*.

S-038
The "Changes Being Effected" supplemental new drug application provides for the addition of 2 new adverse drug reactions identified through postmarketing surveillance. Diabetes mellitus and hypoglycemia have been added to the Postmarketing Experience section.

S-039
The "Prior Approval" supplemental new drug application proposes changes to the previously-agreed class labeling text in the Hyperglycemia and Diabetes Mellitus subsection (Section 5.5) 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 from 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:

> 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.

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

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-21346	SUPPL-39	ORTHO MCNEIL JANSSEN PHARMACEUTICALS INC	RISPERDAL CONSTA(RISPERIDONE)LONG-ACTING
NDA-21346	SUPPL-38	ORTHO MCNEIL JANSSEN PHARMACEUTICALS INC	RISPERDAL CONSTA(RISPERIDONE)LONG-ACTING
NDA-21346	SUPPL-35	ORTHO MCNEIL JANSSEN PHARMACEUTICALS INC	RISPERDAL CONSTA(RISPERIDONE)LONG-ACTING
NDA-21346	SUPPL-31	ORTHO MCNEIL JANSSEN PHARMACEUTICALS INC	RISPERDAL CONSTA(RISPERIDONE)LONG-ACTING

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/s/

THOMAS P LAUGHREN
08/30/2010