CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-304

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-304

NDA APPROVAL

Ortho-McNeil-Janssen Pharmaceuticals, Inc.
c/o Johnson & Johnson Pharmaceutical Research
& Development, L.L.C.
1125 Trenton-Harbourton Road, P.O. Box 200
Titusville, NJ 08560-0200

Attention: Kathleen F. Dusek, R.Ph., RAC
Associate Director, Regulatory Affairs

Dear Ms. Dusek:

Please refer to your new drug application (NDA) dated January 22, 2008, received January 23, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA), for tapentadol.

We acknowledge receipt of your submissions dated March 4, 13, and 19, April 8 and 17, May 5 and 22, June 26 and 27, July 21 and 31, August 1, 8, 20, and 21, September 2, 5, 15, and 16, October 1, and November 5 (2), 10, 11 (2), 18, and 20, 2008.

This new drug application provides for the use of tapentadol tablets for the relief of moderate to severe acute pain.

We have completed our review of this application. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

Your application was not referred to an advisory committee because tapentadol is a member of a class of previously approved opioid drugs and the product did not raise significant safety or efficacy issues beyond those applicable to its class.

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 http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling (text for the package insert and Medication Guide). 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 NDA 22-304**."

CARTON AND IMMEDIATE CONTAINER LABELS

We acknowledge your November 20, 2008, submission containing carton and container labels.

PROPRIETARY NAME

If you choose to use a proprietary name for this product, the name and its use in the labels must conform to the specifications under 21 CFR 201.10 and 201.15. We recommend that you submit any proprietary name to the Agency for our review prior to its implementation. We acknowledge receipt of your submissions dated October 21 and November 14, 2008, concerning a proposed proprietary name. We will convey our decision on your proposal when we have completed our review.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are deferring submission of your pediatric studies until June 30, 2016, because pediatric studies should be delayed until additional safety or effectiveness data have been collected. This delay will allow for accumulation of additional safety information from both the nonclinical juvenile program and the adult postmarketing database prior to initiation of investigation in pediatric patients.

Your deferred pediatric studies required under section 505B(a) of the FDCA are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the FDCA. These required studies are listed below.

1. Treatment of moderate to severe acute pain in pediatric patients ages ≥6 years to ≤17 years.

   You will conduct this trial according to the following timetable:

Protocol Submission:	February 28, 2011
Study Start Date:	March 31, 2011
Final Report Submission:	June 30, 2013

2. Treatment of moderate to severe acute pain in pediatric patients ages birth to <5years.

   You will conduct this trial according to the following timetable:

Protocol Submission:	February 28, 2014
Study Start Date:	March 31, 2014
Final Report Submission:	June 30, 2016

Submit final study reports to this NDA. For administrative purposes, all submissions related to these required pediatric postmarketing studies must be clearly designated:

Required Pediatric Assessment

RISK EVALUATION AND MITIGATION STRATEGIES REQUIREMENTS

Title IX, Subtitle A, Section 901 of the Food and Drug Administration Amendments Act of 2007 (FDAAA) amends the FDCA to authorize FDA to require the submission of a REMS if FDA determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)). This provision took effect on March 25, 2008.

In accordance with section 505-1 of the FDCA, as one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR Part 208. Pursuant to 21 CFR Part 208, FDA has determined that tapentadol poses a serious and significant public health concern requiring the distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of tapentadol. FDA has determined that tapentadol is a product that has serious risks (relative to benefits) of which patients should be made aware because information concerning the risks could affect patients' decision to use, or continue to use, tapentadol. FDA has also determined that tapentadol is a product for which patient labeling could help prevent serious adverse events because of its distinctive properties indicating a high potential for abuse. Under 21 CFR Part 208, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed tapentadol.

Your proposed REMS, submitted on November 18, 2008, and appended to this letter, is approved. The REMS consists of the Medication Guide included with this letter and the timetable for submission of assessments of the REMS included in your November 18, 2008, submission.

Your assessment of the REMS should include:

a. An evaluation of patient understanding of the important risks (i.e., serious adverse events including overdose, misuse, abuse, and accidental exposure) associated with tapentadol

a. A report on periodic assessments of the distribution and dispending of the Medication Guide in accordance with 21 CFR 208.24

b. A report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance

Prominently identify submissions containing REMS assessments or proposed REMS modifications with the following wording in bold capital letters at the top of the first page of the submission:

PREPOSED REMS MODIFICATION
REMS ASSESSMENT
REMS AMENDMENT
REMS - OTHER

CONTROLLED SUBSTANCE SCHEDULING

We have recommended that this product be scheduled under the Controlled Substances Act. We remind you of the following statement that appears on the Form FDA 356h, "If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision." Once a final scheduling decision is made, your label must be amended to reflect the schedule. Submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html. For administrative purposes, designate this submission, "**SPL for approved NDA 22-304.**" Approval of this submission by FDA is not required before the labeling is used.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a form FDA 2253. For instruction on completing form FDA 2253, see page 2 of the form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see www.fda.gov/cder/ddmac.

LETTERS TO HEALTH CARE PROFESSIONALS

If you 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 an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
Suite 12B05
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).

MEDWATCH-TO-MANUFACTURER PROGRAM

The MedWatch-to-Manufacturer Program provides manufacturers with copies of serious adverse event reports that are received directly by the FDA. New molecular entities and important new biologics qualify for inclusion for three years after approval. Your firm is eligible to receive copies of reports for this product. To participate in the program, please see the enrollment instructions and program description details at www.fda.gov/medwatch/report/mmp.htm.

If you have any questions, call Matt Sullivan, Regulatory Project Manager, at 301-796-1245.

Sincerely,

{See appended electronic signature page}

Curtis Rosebraugh, M.D., M.P.H.
Director
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosures:
Package Insert
Medication Guide
Carton and Container
REMS

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Curtis Rosebraugh
11/20/2008 06:45:46 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

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NDA 22-304

CORRECTION TO
NDA APPROVAL LETTER

Ortho-McNeil-Janssen Pharmaceuticals, Inc.
c/o Johnson & Johnson Pharmaceutical Research
& Development, L.L.C.
1125 Trenton-Harbourton Road, P.O. Box 200
Titusville, NJ 08560-0200

Attention: Kathleen F. Dusek, R.Ph., RAC
Associate Director, Regulatory Affairs

Dear Ms. Dusek:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for tapentadol.

We also refer to your labeling submission dated December 15, 2008.

As discussed in your December 2, 2008, telephone conversation with Matthew Sullivan of FDA, tapentadol, which is not currently scheduled under the Controlled Substances Act, was approved on November 20, 2008, with labeling that refers to CSA scheduling. Your December 15 submission includes the package insert and medication guide revised to make a few minor editorial changes, and to exclude the references to CSA scheduling. The carton and immediate container labels have not been revised, because they do not include references to CSA scheduling.

We have completed our review of your December 15 labeling submission and consider this labeling the approved package insert and Medication Guide for this product.

If you have any questions, call Matt Sullivan, Regulatory Project Manager, at (301) 796-1245.

Sincerely,

{See appended electronic signature page}

Curtis Rosebraugh, M.D., M.P.H.
Director
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosures
Package Insert dated December 15, 2008
Medication Guide dated December 15, 2008

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Bob Rappaport
12/24/2008 01:56:44 PM
Signed for Curtis Rosebraugh, M.D.