CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-264

APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-264

NDA APPROVAL

Ortho-McNeil-Jansen Pharmaceuticals, Inc.
Attention: Rodney Malchow
Associate Director, Regulatory Affairs
1125 Trenton-Harbourton Road
P.O. Box 200
Titusville, N.J. 80560

Dear Mr. Malchow:

Please refer to your new drug application (NDA) dated October 25, 2007, received October 26, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Invega Sustenna (paliperidone palmitate) 39mg, 78mg, 117mg, 156mg, and 234 mg extended-release injectable suspension.

We acknowledge receipt of your submissions and communications dated February 2, 2009, February 11, 2009, February 24, 2009, March 24, 2009, May 7, 2009, May 15, 2009, May 20, 2009, May 22, 2009, June 9, 2009, June 22, 2009, June 26, 2009, July 10, 2009, July 15, 2009, July 16, 2009, July 20, 2009 and July 23, 2009.

Your February 2, 2009 submission constituted a complete response to our August 25, 2008 action letter.

This new drug application provides for the use of Invega Sustenna (paliperidone palmitate) extended-release injectable suspension for the acute and maintenance treatment of schizophrenia in adults.

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.

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

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/ForIndustry/DataStandards/StructuredProductLabeling/ucm155657.htm. that is

to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "**SPL for approved NDA 22-264."**

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels as agreed upon in your communication dated July 29, 2009 as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 22-264**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

PROPRIETARY NAME

The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Psychiatry Products do not object to the use of the proprietary name, Invega Sustenna, for this product.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens 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 waiving the pediatric study requirement for ages 0 to 12 years because necessary studies are impossible or highly impracticable due to the very low incidence of schizophrenia diagnosed prior to age 13.

We are deferring submission of your pediatric studies for ages 13 to 17 years because pediatric studies in this age group should be delayed until additional safety and effectiveness data have been collected. Studies for the extended-release injectable suspension are deferred until studies currently being conducted under the adolescent schizophrenia development program are complete.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act 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 Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

1. A deferred pediatric study under PREA for the treatment of schizophrenia in pediatric patients

dosing of paliperidone palmitate extended-release injectable suspension in the relevant pediatric population. This study will be initiated after submission of the reports from the ongoing pediatric oral paliperidone studies to support use of paliperidone in adolescents aged 13 – 17.

Final Protocol Submission:	by June 1, 2011
Study Completion Date:	by November 1, 2013
Final Report Submission:	by January 1, 2014

2. A deferred pediatric study under PREA for the treatment of schizophrenia in pediatric patients ages 13 to 17. A study of the efficacy and safety of paliperidone palmitate extended-release injectable suspension in the relevant pediatric population.

Final Protocol Submission:	by November 1, 2013
Study Completion Date:	by April 1, 2015
Final Report Submission:	by October 1, 2016

Submit clinical protocols to your IND for this product. Submit final reports to your NDA 22-264. Use the following designator to prominently label all submissions:

Required Pediatric Assessment(s)

POSTMARKETING COMMITMENTS NOT SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of the following postmarketing commitment agreed upon in our communication dated July 20, 2009.

3. You have committed to adding a clearly visible fill line to the syringe barrel so that the health care provider can ensure that the syringes contain the required volume of suspension prior to administration and that no gross leakage or evaporation of the syringe contents has occurred during storage or shipping. We request that this change be carried out, and a prior approval supplement be submitted within one year of approval.

Completion date: by August 2010

Under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to this postmarketing study commitment should be prominently labeled "**Postmarketing Commitment Protocol**", "**Postmarketing Commitment Final Report**", or "**Postmarketing Commitment Correspondence**."

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 the 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.

DISSOLUTION METHOD AND SPECIFICATIONS

The dissolution method and specifications for all strengths of the extended-release injectable suspension should be:

Parameter	**Dissolution Method and Specification**	
Apparatus Type	USP Type II (paddle)	
Media	0.001 M HCl containing 0.489% Polysorbate 20 (Tween®20)	
Volume	900 ml	
Temperature	25 ± 0.5 °C	
Frequency	50 rpm	
Sampling Times	1.5, 8, 20, and 45 minutes	
Acceptance Criteria	1.5 minutes	NMT (b) (4) of Label Claim
	8 minutes	(b) (4) of Label Claim
	20 minutes	(b) (4) of Label Claim
	45 minutes	(b) (4) of Label Claim
Analysis	HPLC UV detection	

EXPIRY

A 24 month expiry date is granted based on the available stability data.

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 a copy to the following address:

MedWatch
Food and Drug Administration
Suite 12B05
5600 Fishers Lane

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.