CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

022264Orig1s012

Trade Name:	**Invega Sustenna**
Generic or Proper Name:	(paliperidone palmitate)
Sponsor:	Janssen Pharmaceuticals Inc
Approval Date:	August 25, 2014
Indication:	Invega Sustenna is an atypical antipsychotic indicated for: • Treatment of schizophrenia • Treatment of schizoaffective disorder as monotherapy and as an adjunct to mood stabilizers or antidepressants

CENTER FOR DRUG EVALUATION AND RESEARCH

022264Orig1s012

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Reviews / Information Included in this NDA Review.

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Clinical Review(s)	
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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

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APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22-264/S-012

APPROVAL LETTER

Janssen Pharmaceuticals, Inc.
c/o Janssen Research and Development, L.L.C
Attention: Beth Geter-Douglass, Ph.D., Associate Director, Global Regulatory Affairs
920 Route 202, P.O. Box 300
Raritan, NJ 08869

Dear Dr. Geter-Douglass:

Please refer to your supplemental new drug application dated April 25, 2014, received April 25, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Invega Sustenna (paliperidone palmitate) extended-release injectable suspension for intramuscular use.

This "Prior Approval" supplemental new drug application provides for amending DMF 20902 to remove testing of genotoxic impurity (b) (4) and (b) (4)

We completed our review of this supplemental new drug application and it is approved.

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

If you have any questions, call Teshara G. Bouie, Regulatory Health Project Manager, at (301) 796-1649.

Sincerely,

{See appended electronic signature page}

Hasmukh Patel, Ph.D.
Branch Chief
Branch III, Division of New Drug Quality Assessment I
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

NALLAPERUM CHIDAMBARAM
08/25/2014
for Dr. Hasmukh Patel

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022264Orig1s012

PRODUCT QUALITY REVIEW(S)

Review of Chemistry, Manufacturing, and Controls

Clinical Review Division: Division of Psychiatry Products

NDA #: 22-264 **CHEM. REVIEW #:** 1 **REVIEW DATE:** 08/19/14

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE	DUE DATE
N 22264/S-012 (PA)	04/25/14	04/25/14	05/13/14	08/25/14

NAME & ADDRESS OF APPLICANT: Ortho-McNeil-Janssen Pharm., Inc. (Applicant)
Agent: Johnson & Johnson Pharmaceutical R&D, L.L.C.
920 Route 202, P.O. Box 300
Raritan, NJ 08869

DRUG PRODUCT NAME

Proprietary: INVEGA Sustenna
Nonproprietary/USAN: Paliperidone palmitate

Patent Status: NA

PHARMACOLOGICAL CATEGORY/INDICATION: Maintenance of stability in schizophrenic patients

DOSAGE FORM: Suspension (extended-release) (sterile)

STRENGTHS: 38mg, 78mg, 117mg, 156mg, and 234mg Paliperidone palmitate suspension

ROUTE OF ADMINISTRATION: Intramuscular injection

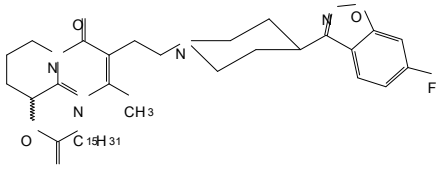
DISPENSED: Rx

PACKAGE SIZES:

SPECIAL PRODUCTS: ☐ Yes ☒ No (If yes, fill out the form for special products and deliver to TIA through team leader for data entry)

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOL. WT:

Chemical Name: (±)-3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl-4-oxo-4*H*-pyrido[1,2a]pyrimidin-9-yl hexadecanoate
Molecular Wt.: 664.89
Molecular Formula: $C_{39}H_{57}FN_4O_4$



PALIPERIDONE PALMITATE

SUPPORTING DOCUMENTS: NA

RELATED DOCUMENTS: DMF Review dated 19-AUG-2014

CONSULTS: Microbiology Review dated 28-JUL-2014

REMARKS/COMMENTS:

This Prior Approval Supplement supplement provides for removal of testing for genotoxic impurity [redacted] (b) (4) and [redacted] (b) (4) in the R092670 (paliperidone palmitate) "sterile grade" drug substance specification. The detailed knowledge of the origin and fate of potentially genotoxic impurities in the paliperidone palmitate synthesis, the supporting data from commercial drug substance batches, and the assessments performed in the firm's quality systems with regard to the impact of any future process change on potential genotoxic impurity levels have been described in an amendment to DMF 20902 in order to justify the proposed removal of testing for genotoxic impurity and [redacted] (b) (4) n the drug substance specifications.

DMF 20902 has been reviewed as sanctioned by the firm's Letter of Authorization. The DMF has been determined to be Adequate, which permits approving this request.

Review by Microbiology indicated that no action is indicated because removal of testing for genotoxic impurity (b) (4) and (b) (4) would have no impact on sterility assurance.

CONCLUSIONS & RECOMMENDATIONS: The CMC information presented in the submission is sufficient to recommend APPROVAL of this supplement.

cc: Orig. NDA 22-264
DMIHP/Division File
DMIHP/CSO/TBouie

filename: n22264s.012.doc

Allan Fenselau, Ph.D., Review Chemist

DRAFT SUPPLEMENT LETTER

There are no CMC–specific deficiencies; therefore, no draft letter was generated.

REVIEW NOTES

INTRODUCTION

This Prior Approval Supplement supplement requests to make changes that are described in an amendment to paliperidone palmitate Type II DMF 20902, submitted on April 23, 2014, for which this NDA is authorized to refer to for current and future information on paliperidone palmitate drug substance. [The specific changes are not identified in the supplement Cover Letter; however, details are provided in a section of the supplement entitled "*Summary of Basis Statement*."]

This submission provides for removal of testing for genotoxic impurity (b) (4) and (b) (4) (b) (4) in the R092670 (paliperidone palmitate) "sterile grade" drug substance specification. The detailed knowledge of the origin and fate of potentially genotoxic impurities in the paliperidone palmitate synthesis, the supporting data from commercial drug substance batches, and the assessments performed in the firm's quality systems with regard to the impact of any future process change on potential genotoxic impurity levels are described in this amendment in order to justify the proposed removal of testing for genotoxic impurity (b) (4) and (b) (4) in the R092670 "sterile grade" drug substance specification.

> [NOTE: *The sponsor should be informed that, per regulations in the CFR, the Cover Letter to the sNDA should contain a list of all changes being requested*.]

DMF 20902 has been reviewed by ONDQA Reviewer Dr. A. Fenselau as sanctioned by the firm's Letter of Authorization dated 23-APR-2014. The DMF has been determined to be Adequate, which permits approving this request.

1. Microbiology **APPROVED**

The Microbiology review by Dr. V. Viehmann (dated 28-JUL-2014) indicated that no action is indicated because removal of testing for genotoxic impurity (b) (4) and (b) (4) would have no impact on sterility assurance.

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/s/

ALLAN H FENSELAU
08/19/2014

HASMUKH B PATEL
08/19/2014

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022264Orig1s012

OTHER REVIEW(S)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Office/Division)*: Vera Viehmann, OPS/ New Drug Microbiology			FROM *(Name, Office/Division, and Phone Number of Requestor)*: Teshara G. Bouie, ONDQA, Division of New Quality Assessment I, 301-796-1649	
DATE July 18, 2014	IND NO.	NDA NO. 22-264	TYPE OF DOCUMENT S-012	DATE OF DOCUMENT April 25, 2014
NAME OF DRUG Invega Sustenna	PRIORITY CONSIDERATION		CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE August 11, 2014

NAME OF FIRM: Janssen Pharmaceuticals

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☒ MANUFACTURING CHANGE / ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE-NDA MEETING
- ☐ END-OF-PHASE 2a MEETING
- ☐ END-OF-PHASE 2 MEETING
- ☐ RESUBMISSION
- ☐ SAFETY / EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☐ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

- ☐ PRIORITY P NDA REVIEW
- ☐ END-OF-PHASE 2 MEETING
- ☐ CONTROLLED STUDIES
- ☐ PROTOCOL REVIEW
- ☐ OTHER (SPECIFY BELOW):
- ☐ CHEMISTRY REVIEW
- ☐ PHARMACOLOGY
- ☐ BIOPHARMACEUTICS
- ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE 4 STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL - BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG SAFETY

- ☐ PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ NONCLINICAL

COMMENTS / SPECIAL INSTRUCTIONS: The referenced DMF 20902 amendment describes a major change to the manufacturing process, the introduction of the (b) (4) processing of R092670 "sterile grade" drug substance at the Cork facility as an alternative to the current (b) (4) batch process. Please review.

PDUFA Goal Date: August 25, 2014

SIGNATURE OF REQUESTOR Teshara G. Bouie	METHOD OF DELIVERY (Check one) ☒ DARRTS ☐ EMAIL ☐ MAIL ☐ HAND
PRINTED NAME AND SIGNATURE OF RECEIVER	PRINTED NAME AND SIGNATURE OF DELIVERER

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/s/

TESHARA G BOUIE
07/18/2014

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022264Orig1s012

ADMINISTRATIVE AND CORRESPONDENCE DOCUMENTS

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 22-264/S-012

ACKNOWLEDGEMENT --
PRIOR APPROVAL SUPPLEMENT

Janssen Pharmaceuticals, Inc.
Attention: Beth Geter-Douglass, Ph.D.
Associate Director, Global Regulatory Affairs
1125 Trenton-Harbourton Rd., E11710
Titusville, NJ 08560

Dear Dr. Geter-Douglass:

We have received your Supplemental New Drug Application (sNDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA or the Act) for the following:

NDA NUMBER: 22-264

SUPPLEMENT NUMBER: S-012

PRODUCT NAME: Invega Sustenna (paliperidone palmitate) Extended Release Injection

DATE OF SUBMISSION: April 25, 2014

DATE OF RECEIPT: April 25, 2014

This supplemental application provides for an amendment to DMF 20902 to remove testing of genotoxic impurity (b) (4) and (b) (4)

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on June 24, 2014, in accordance with 21 CFR 314.101(a).

If the application is filed, the user fee goal date will be August 25, 2014.

SUBMISSION REQUIREMENTS

Cite the application number listed above at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

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

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, see http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm.

If you have any questions, call me, at (301) 796-1649.

Sincerely,

{See appended electronic signature page}

Teshara G. Bouie, MSA, OTR/L
CDR, USPHS, Regulatory Health Project Manager
Division of New Drug Quality Assessment I
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

TESHARA G BOUIE
05/23/2014