

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

022264Orig1s011

Trade Name: **Invega Sustenna**
Generic or Proper Name: (paliperidone palmitate)

Sponsor: Janssen Pharmaceuticals Inc

Approval Date: August 26, 2013

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

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APPROVAL LETTER



NDA 22264/S-011

APPROVAL LETTER

Janssen Pharmaceuticals, Inc.
c/o Janssen Research and Development L.L.C.
Attention: Kate Huddleston, Manager, Global Regulatory Affairs
920 Route 202
P.O. Box 300
Raritan, NJ 08869

Dear Ms. Huddleston:

Please refer to your Supplemental New Drug Application (sNDA) dated April 25, 2013, received April 26, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for INVEGA Sustenna (paliperidone palmitate) Injection.

This "Prior Approval" supplemental new drug application provides for the change in the manufacturing process of R092670 "sterile grade" drug substance at the Janssen Pharmaceutical, Cork, Ireland facility.

We have completed our review of this supplemental new drug application. This supplement is approved.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

Sincerely,

{See appended electronic signature page}

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

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/s/

HASMUKH B PATEL
08/26/2013

**CENTER FOR DRUG EVALUATION AND
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APPLICATION NUMBER:

022264Orig1s011

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:** 08/09/13

SUBMISSION TYPE	DOCUMENT DATE	CDER DATE	ASSIGNED DATE	DUE DATE
N 22264/S-011 (PA)	04/25/13	04/26/13	6/25/13	08/26/13

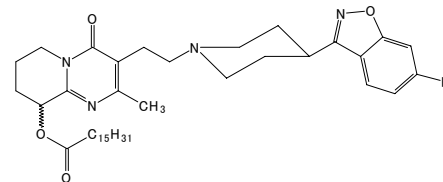
NAME & ADDRESS OF APPLICANT: Ortho-McNeil-Janssen Pharm., Inc. (Applicant)
 Agent: Johnson & Johnson Pharmaceutical R&D, L.L.C.
 920 Route 202, P.O. Box 300
 Raritan, NJ 08869

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:** R_x**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-4H-pyrido[1,2a]pyrimidin-9-yl hexadecanoate
 Molecular Wt.: 664.89
 Molecular Formula: C₃₉H₅₇FN₄O₄

**PALIPERIDONE PALMITATE****SUPPORTING DOCUMENTS:** NA**RELATED DOCUMENTS:** DMF Reviews dated 22-JUL-2013 and 09-AUG-2013**CONSULTS:** Microbiology Consult dated 22-JUL-2013**REMARKS/COMMENTS:**

This Prior Approval Supplement supplement requests approval for a change in the manufacturing process of R092670 “sterile grade” drug substance at the Janssen Pharmaceutical, Cork, Ireland facility. The change consists of the introduction of (b) (4) R092670 “sterile grade” drug substance batches at commercial scale at the Cork facility as an alternative to the current (b) (4) batch process. The change is described in an amendment to paliperidone palmitate Type II DMF 20902, submitted on 02-APR-2013 (a Letter of Authorization has been provided in order to refer to for current and future information on paliperidone palmitate drug substance). No other changes have been requested.

The proposal in the DMF has been reviewed by CMC and Microbiology and the proposal (as well as the other CMC updates) have been found to be Adequate.

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.011.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 approval for the change in the manufacturing process of R092670 "sterile grade" drug substance at the Janssen Pharmaceutical, Cork, Ireland facility. The change consists of the introduction of (b) (4) R092670 "sterile grade" drug substance batches at commercial scale at the Cork facility as an alternative to the current (b) (4) batch process. The change is described in an amendment to paliperidone palmitate Type II DMF 20902, submitted on 02-APR-2013 (a Letter of Authorization has been provided in order to refer to for current and future information on paliperidone palmitate drug substance).

No other changes have been submitted.

1. Manufacturing Process

ACCEPTABLE

Examination of this submission indicated that the Division of Microbiology needs to be consulted on the acceptability of this proposal. The following consult request was forwarded to them:

Janssen is proposing (in NDA 22264/S-011) to make the following change (as a Prior Approval Supplement) to the manufacturing process of R092670 "sterile grade" drug substance at the Janssen Pharmaceutical, Cork, Ireland facility [see DMF 20902/Amendment dated 02-APR-2013]. The approved process for manufacturing sterile grade drug substance (b) (4) is shown below, but it excludes the operations included in the box with bold borders (b) (4). Their proposed modification is to (b) (4)

(b) (4) The submission updates the DMF sections describing this change. No sterility data for batches subjected to this treatment have been provided. [01-JUL-2013]

Is there need for a Micro review?

R092670 "Sterile Grade" Drug Substance (b) (4) Process
(b) (4) Sterile Batches

The inquiry produced the review cited above (Microbiology Review dated 22-JUL-2013). The reviewer's (Dr. D. Miller) recommendation was that DMF 20902 is acceptable in support of NDA 022-264/S011.

Full information on this recommendation can be found in the DMF 20902 Microbiology Review (dated 22-JUL-2013). An updated CMC review of the DMF (as of the date of an Annual Report submitted on 23-JUL-2013) has also been conducted 09-AUG-2013) and has concluded the DMF remains adequate to support NDA 22264.

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/s/

ALLAN H FENSELAU
08/09/2013

HASMUKH B PATEL
08/09/2013

Product Quality Microbiology Review

22 July 2013

NDA: 022-264/S011

Drug Product Name

Proprietary: INVEGA SUSTENNA

Non-proprietary: Paliperidone palmitate

Review Number: 1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
25 April 2013	26 April 2013	2 July 2013	05 July 2013

Submission History (for 2nd Reviews or higher) – NA

Applicant/Sponsor

Name: Janssen Pharmaceuticals, Inc.

Address: 1125 Trenton-Harbourton Rd
Titusville, N.J. 08560

Representative: Catherine Huddleston
Manager, Global Regulatory Affairs

Telephone: (908) 704-5668

Name of Reviewer: Denise A. Miller

Conclusion: Recommended for Approval

Product Quality Microbiology Data Sheet

- A.**
- 1. TYPE OF SUBMISSION:** Prior Approval
 - 2. SUBMISSION PROVIDES FOR:** Changes in the Type II DMF 20902 for the sterile drug substance.
 - 3. MANUFACTURING SITE:** No change
 - 4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY:**
 - Dosage Form: sterile suspension for injection in a pre-filled syringe.
 - Route of Administration: Intramuscular
 - Strength/Potency: 39, 78, 117, 156, and 234 mg/ syringe
 - 5. METHOD(S) OF STERILIZATION:** (b) (4)
 - 6. PHARMACOLOGICAL CATEGORY:** Acute and maintenance treatment of Schizophrenia.
- B. SUPPORTING RELATED DOCUMENTS:**
Type II DMF 20902 Paliperidone Palmitate (R092670) Drug Substance; reviewed by NDMS on 22 July 2013 and found to be adequate.
- C. REMARKS:**
1) The format of the submission is e-CTD.

filename: N022264S011R1.doc

Executive Summary

I. Recommendations

- A. Recommendation on Approvability** - Recommended for Approval.
- B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable** - NA

II. Summary of Microbiology Assessments

- A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology** – The drug product is (b) (4)
(b) (4)
(b) (4) There is no change to the drug product manufacturing submitted in this supplement.
- B. Brief Description of Microbiology Deficiencies** – None identified.
- C. Assessment of Risk Due to Microbiology Deficiencies** – NA
- D. Contains Potential Precedent Decision(s)**- Yes No
(If yes, provide a brief description and a reference to the page where the precedent is discussed in depth)

III. Administrative

- A. Reviewer's Signature** _____
Denise A. Miller
Microbiologist, OPS/NDMS
- B. Endorsement Block** _____
Bryan S. Riley, Ph.D.
Senior Microbiologist, OPS/NDMS
- C. CC Block**
N/A

Product Quality Microbiology Assessment

This supplement is a Prior Approval Supplement for a change submitted to DMF 20902. The change for the sterile drug substance submitted to DMF 20902 was reviewed by the New Drug Microbiology Staff on 18 July 2013 and found to be acceptable in support of NDA 022-264/S011. There were no other changes submitted.

-ADEQUATE-

Reviewer's comment: DMF 20902 is acceptable in support of NDA 022-264/S011.

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/s/

DENISE A MILLER
07/22/2013

BRYAN S RILEY
07/22/2013
I concur.

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022264Orig1s011

OTHER REVIEW(S)

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

CMC MICRO & STERILITY ASSURANCE REVIEW REQUEST

TO (*Division/Office*): **New Drug Microbiology Staff**

***E-mail to:* CDER OPS IO MICRO**
***Paper mail to:* WO Bldg 51, Room 4193**

FROM:

Yvonne Knight, ONDQA, Division of New Drug
Quality Assessment I (301) 796-2133

PROJECT MANAGER (*if other than sender*):

REQUEST DATE
7/2/13

IND NO.

NDA NO.
22264

TYPE OF DOCUMENT
Supplement 011

DATE OF DOCUMENT
4/26/13

NAMES OF DRUG
Invega Sustenna (apikiperidone
palmitate) suspension injection

PRIORITY CONSIDERATION
PAS

PDUFA DATE
8/26/13

DESIRED COMPLETION DATE
8/12/13

NAME OF APPLICANT OR SPONSOR: Janssen Pharmaceuticals Inc.

GENERAL PROVISIONS IN APPLICATION

- | | |
|---|---|
| <input type="checkbox"/> 30-DAY SAFETY REVIEW NEEDED | <input type="checkbox"/> CBE-0 SUPPLEMENT |
| <input type="checkbox"/> NDA FILING REVIEW NEEDED BY: _____ | <input type="checkbox"/> CBE-30 SUPPLEMENT |
| <input type="checkbox"/> BUNDLED | <input type="checkbox"/> CHANGE IN DOSAGE, STRENGTH / POTENCY |
| <input type="checkbox"/> DOCUMENT IN EDR | |

COMMENTS / SPECIAL INSTRUCTIONS:

DMF 20902 amendment provides for a change to the manufacturing process of R092670 "sterile grade" drug substance at the Janssen Pharmaceutical, Cork, Ireland facility.

SIGNATURE OF REQUESTER

REVIEW REQUEST DELIVERED BY (Check one):

DARRTS EDR E-MAIL MAIL HAND

Reference ID: 3335205

DOCUMENTS FOR REVIEW DELIVERED BY (Check one):

EDR E-MAIL MAIL HAND

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/s/

YVONNE L KNIGHT
07/02/2013