CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

022264Orig1s017

Trade Name:	**Invega Sustenna**
Generic or Proper Name:	(paliperidone palmitate)
Sponsor:	Janssen Pharmaceuticals Inc
Approval Date:	June 15, 2015
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

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022264Orig1s017

APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22264/S-017

APPROVAL LETTER

Janssen Pharmaceuticals, Inc.
c/o Janssen Research and Development, L.L.C.
Attention: Beth Geter-Douglass, Ph.D., Associate Director, Regulatory Affairs
1125 Trenton-Harbourton Rd.
Titusville, NJ 08560

Dear Dr. Geter-Douglas:

Please refer to your Supplemental New Drug Application (sNDA) dated December 16, 2014, received December 16, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Invega Sustenna (paliperidone palmitate) extended-release injectable suspension.

This "Changes Being Effected in 30 days" supplemental new drug application provides for a change to the manufacturing process of R092670 "sterile grade" drug substance which is described in an amendment to paliperidone palmitate Type II DMF 20902.

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.

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

Sincerely,

David Lewis, Ph.D., CMC Lead, on behalf of:

Hasmukh Patel, Ph.D.
Division Director (Acting)
Division of Post Marketing Activities I
Office of Lifecycle Drug Products
Office of Pharmaceutical Quality
Center for Drug Evaluation and Research

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022264Orig1s017

PRODUCT QUALITY REVIEW(S)

Office of Pharmaceutical Quality
Office of Lifecycle Drug Product (OLDP)
Division of Post Marketing Activities I (Branch II)
Review of Chemistry, Manufacturing, and Controls

1. **NDA number: 22264**

2. **Submission(s) Being Reviewed**

Supplement Number	eCTD Sequence #	Submission Date	CDER Stamp Date	Assigned Date	PDUFA Goal Date	Review Date
S-017 CBE-30	0142	12/16/2014	12/16/2014	1/16/2015	6/16/2015	6/12/2015

3. **Proposed Changes:** This CBE-30 supplement provides for a change to the manufacturing process of R092670 "sterile grade" drug substance which is described in an amendment to paliperidone palmitate Type II DMF 20902.

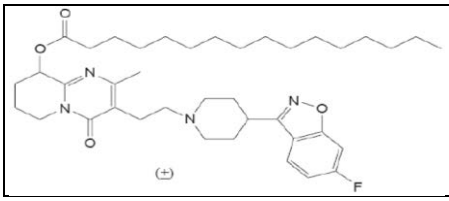
4. **Review #1**
5. **Clinical Review Division:** CDER/ODEI/DPP
6. **Name and Address of Applicant:**
   Janssen Research and Development, L.L.C. of behalf of Janssen Pharmaceuticals, Inc.
   1125 Trenton-Harbourton Rd, P.O. Box 200
   Titusville, NJ 08560

7. **Drug Product:**

Proprietary Name	Nonproprietary Name (USAN) of Drug Substance	Indication	Dosage Form	Strength	Route of Administration
INVEGA SUSTENNA	Paliperidone Palmitate	Schizophrenia Schizoaffective disorder	Extended Release Injectable Suspension	39,78,117,156, 234 mg	Intramuscular Injection

Rx or OTC	Special Product?
Rx	No

8. **Chemical name and structure of drug substance:**



Chemical name: (±)-3-[2-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl]-6,7,8,9-tetrahydro-2-methyl4-oxo-4*H*-pyrido[1,2-*a*]pyrimidin-9-yl hexadecanoate
Molecular formula: $C_{39}H_{57}FN_4O_4$
MW: 664.89

9. **Supporting/Relating Document:** DMF 20902

10. Consults: Pharmacology/toxicology (unofficial consult).

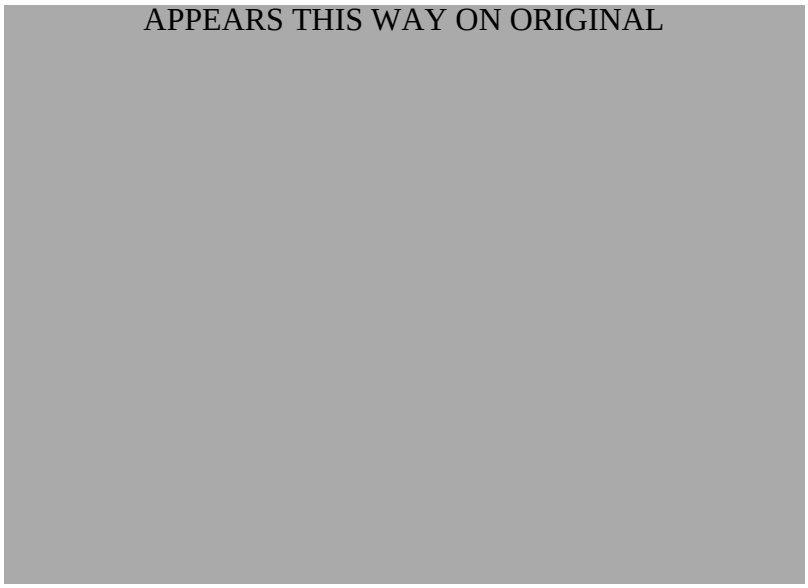
Summary/Remarks: This CBE-30 Supplement for NDA 22264 provides for changes which are described in an amendment to paliperidone palmitate Type II DMF 20902, submitted on 11/04/2014. The LOA for FDA to access this DMF which is referred for NDA 22264 is provided (10/23/2014). The DMF 20902 has been reviewed recently, in support of NDA 207-946, Invega Trinza™, paliperidone palmitate 200 mg/mL extended-release suspension for injection and was found to be adequate to support that NDA [Quality review dated 3/10/2015, by Monica Cooper, Ph.D. (adequate with information request)]. The same API and the same manufacturing process are used in both formulations for two NDAs. The Information Request for DMF was made regarding the proper calculations of the concentration limits for genotoxic impurities in the final drug substance. Based on the informal consultation with the pharmacology/toxicology team (DPP), the same limit of each genotoxic impurity is recommended for both formulations used in the NDA 22-264 and NDA 207-946, even though the drug product in NDA 22-264 is used at a lower dose and shorter duration of action than that in NDA 207-946, i.e., 156 mg/ml once per month injection for Invega Sustenna® vs. 312 mg/ml once every 3 months injection for Invega Trinza™. Therefore, the limits for genotoxic impurities that will be accepted in DMF 20902 reviewed for NDA 207-946 are acceptable for NDA 22-264. The microbiology consult has been requested to review DMF amendment dated 11/04/2014, and it also was found to be adequate (Microbiology review dated 3/23/2015, Kristy L. McDowell, Ph.D.). The NDA applicant for 22-264 and 207-946 belongs to the same group of companies as the DMF 20902 holder (Janssen Pharmaceuticals Companies). Based on the adequacy of the referenced DMF 20902, determined by the Microbiology reviewer for this particular Supplement, adequacy of DMF 20902 determined by the Quality reviewer, and based on communication with pharm/tox team this Supplement can be recommended for Approval.

11. Conclusions & Recommendations: Recommend Approval from CMC perspective.

12. Comments/Deficiencies to be Conveyed to Applicant: None.

13. Primary Reviewer: Lyudmila Soldatova, Ph.D., Quality Reviewer, Division of Post-Marketing Activities I (DPMA1), Office of Lifecycle Drug Products (OLDP), Office of Pharmaceutical Quality (OPQ)

Secondary Reviewer: Signing for Hasmukh Patel, Ph.D., DMPA1 Branch 2 Chief, OLDP, OPQ


APPEARS THIS WAY ON ORIGINAL

Product Quality Microbiology Review

March 12, 2015

NDA: 22-264/S-017

Drug Substance Name
Proprietary: INVEGA SUSTENNA
Non-proprietary: Paliperdone palmitate

Review Number: #1

Dates of Submission(s) Covered by this Review

Submit	Received	Review Request	Assigned to Reviewer
16 Dec. 2014	16 Dec. 2014	21 Jan. 2015	22 Jan. 2015

Applicant/Sponsor
Name: Janssen Research and Development, L.L.C. of behalf of Janssen Pharmaceuticals, Inc.
Address: 1125 Trenton-Harbourton Rd. P.O Box 200, Titusville, New Jersey 08560
Representative: Wendy Mavroudakis
Telephone: 609-730-3067
Fax: 609-730-2706

Name of Reviewer: Kristy L. McDowell, PhD

Conclusion: Recommended for Approval

Product Quality Microbiology Data Sheet

A. 1. TYPE OF SUBMISSION: Supplement CBE30

2. SUBMISSION PROVIDES FOR: A reduction in (b) (4) monitoring sites for routine equipment (b) (4)

3. MANUFACTURING SITE:
Janssen Pharmaceutical
Wallinton
Little Island, County Cork
Republic Of Ireland

4. DOSAGE FORM, ROUTE OF ADMINISTRATION AND STRENGTH/POTENCY: Extended Release Injectable Suspension; Intramuscular Injection; 39, 78, 117, 156, 234 mg

5. METHOD(S) OF STERILIZATION: (b) (4)

6. PHARMACOLOGICAL CATEGORY: Treatment of schizophrenia and schizoaffective disorder

B. SUPPORTING/RELATED DOCUMENTS: See the microbiology review of DMF 020902 dated March 12, 2015.

C. REMARKS: This supplement was in the eCTD format.

Filename: 022264s17.doc

Executive Summary

I. Recommendations

A. Recommendation on Approvability - Recommended for Approval.

B. Recommendations on Phase 4 Commitments and/or Agreements, if Approvable – N/A

II. Summary of Microbiology Assessments

A. Brief Description of the Manufacturing Processes that relate to Product Quality Microbiology – This is (b) (4) sterile drug substance.

B. Brief Description of Microbiology Deficiencies – None identified

C. Contains Potential Precedent Decision(s) - ☐ **Yes** ☒ **No**

III. Administrative

A. Reviewer's Signature _____

B. Endorsement Block

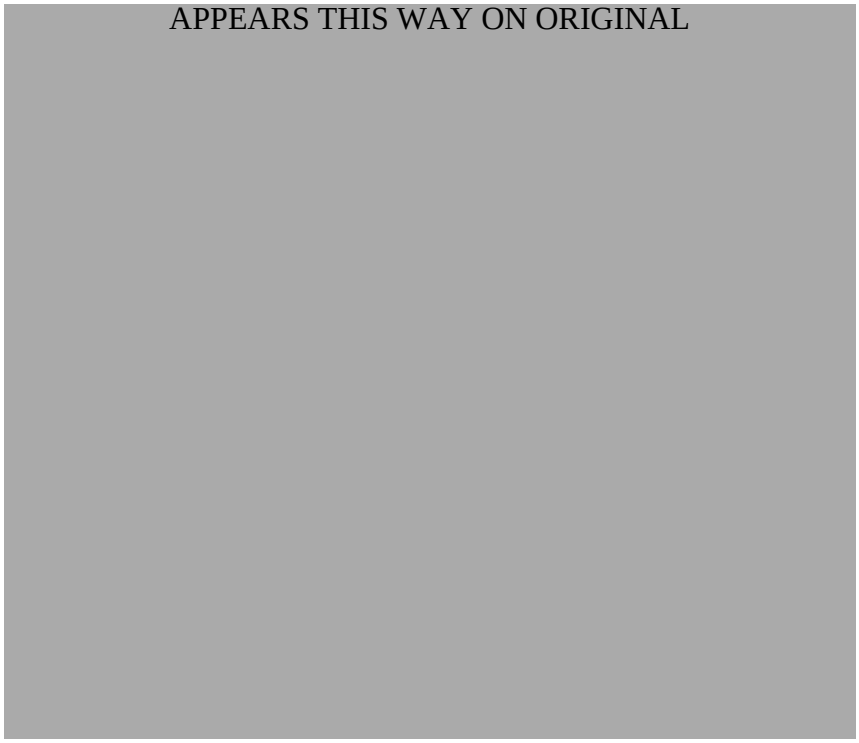
Microbiologist: Kristy L. McDowell, Ph.D.
Microbiology Secondary Reviewer: Jessica Cole, Ph.D.
Microbiology Branch Chief: Stephen Langille, Ph.D.

Product Quality Microbiology Assessment

The March 11, 2015 review of DMF 020902 found the information adequate to support approval of the reduction in monitoring sites for routine equipment (b) (4) (b) (4)

LIST OF MICROBIOLOGY DEFICIENCIES AND COMMENTS:

None.


APPEARS THIS WAY ON ORIGINAL