



NDA 21999/S-029  
NDA 22264/S-010

**SUPPLEMENT APPROVAL**

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

Dear Dr. Geter-Douglas:

Please refer to your Supplemental New Drug Applications (sNDAs) dated April 25, 2013 and received April 26, 2013, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Invega (paliperidone) tablets, and Invega Sustenna (paliperidone) extended-release suspension for intramuscular injection.

We acknowledge receipt of your amendments dated November 12, 2013.

The November 12, 2013 submissions constituted a complete response to our September 25, 2013, action letter.

These "Prior Approval" supplemental new drug applications propose the following:

1. Text to clarify that carbamazepine is a strong inducer of both CYP3A4 and P-glycoprotein in the INVEGA<sup>®</sup> and INVEGA<sup>®</sup> SUSTENNA<sup>®</sup> labels
2. The addition of the term "ileus" to the appropriate alphabetical location in the sentence that lists adverse reactions in the Postmarketing Experience sections of the INVEGA<sup>®</sup> and INVEGA<sup>®</sup> SUSTENNA<sup>®</sup> labels.
3. The addition of the following sentence to the INVEGA<sup>®</sup> SUSTENNA<sup>®</sup> label, Section 6.2: "Very rarely, cases of anaphylactic reaction after injection with INVEGA<sup>®</sup> SUSTENNA<sup>®</sup> have been reported during postmarketing experience in patients who have previously tolerated oral risperidone or oral paliperidone."

**APPROVAL & LABELING**

We have completed our review of these supplemental applications. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

## **CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling (text for the package insert), with the addition of any labeling changes in pending “Changes Being Effectuated” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled “SPL Standard for Content of Labeling Technical Qs and As at <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

## **REPORTING REQUIREMENTS**

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

If you have any questions, please email Ann Sohn, Regulatory Project Manager, at [ann.sohn@fda.hhs.gov](mailto:ann.sohn@fda.hhs.gov).

Sincerely,

*{See appended electronic signature page}*

Mitchell V. Mathis, M.D.  
CAPT, USPHS  
Director  
Division of Psychiatry Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

ENCLOSURE:  
Content of Labeling

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**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
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/s/  
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MITCHELL V Mathis  
04/29/2014