CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-264

OTHER REVIEW(S)

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology

Date:	July 10, 2009
To:	Thomas Laughren, MD, Director Division of Psychiatry Products
Through:	Laura Pincock, R.Ph, PharmD, Acting Team Leader Denise Toyer, PharmD, Deputy Director Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis
From:	Diane C. Smith, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis
Subject:	Label and Labeling Review
Drug Name(s):	Invega Sustenna (Paliperidone Palmitate) Injection 25 mg, 50 mg, 75 mg, 100 mg and 150 mg
Application Type/Number:	NDA 22-264
Applicant/Sponsor:	Janssen, Division of Ortho-McNeil-Janssen Pharmaceuticals, Inc.
OSE RCM #:	2009-286

Contents

1 EXECUTIVE SUMMARY

Invega Sustenna (Paliperidone Palmitate) is an extended release intramuscular injection for the acute and maintenance treatment of schizophrenia in adults. Invega Sustenna is a product line extension of Invega (Paliperidone) oral tablets. Paliperidone palmitate is an ester of paliperidone and is dosed based upon the palmitate ester according to CMC. As such, DMEPA considered the vulnerability of labeling the product strength based on the ester paliperidone palmitate as compared to labeling the product strength in terms of milligram equivalents of paliperidone.

The findings of our Label and Labeling Risk Assessment indicate that improvements can be made prior to approval to the presentation of the product strength, proprietary name, established name, and the dosage form statement on the container labels and carton labeling to provide consistency and reduce the likelihood of confusion. We provide recommendations in Section 5.2 that aim at reducing the risk of medication errors.

2 REGULATORY HISTORY

The Division of Medication Error Prevention and Analysis previously reviewed the applicant's labels and labeling for the proposed name, Invega Sustenna, in OSE Review # 2008-117, dated August 5, 2008. This review noted the expression of strength on the labels and labeling was inconsistent with the dose provided in the Dosage and Administration Section of the labeling. Specifically, we recommended the Applicant avoid the term "milligram equivalents" or the abbreviation "mg eq". Subsequently on October 21, 2008, the applicant submitted a Complete Response Briefing Book, which contained justification to present the product strengths in terms of milligram (mg) paliperidone equivalent. The applicant noted that confusion could arise if the product strengths were presented in terms of paliperidone palmitate versus mg paliperidone equivalents.

3 MATERIALS REVIEWED

Revised container labels and carton labeling were submitted on February 2, 2009. The Division of Medication Error Prevention and Analysis (DMEPA) used Failure Mode and Effects Analysis (FMEA) in our evaluation of these labels and labeling. We also reviewed the justification provided by the Applicant contained in the Complete Response Briefing Book, dated October 21, 2008. See Appendix A through E for images.

4 DISCUSSION

The Applicant was requested to label this product using the “mg” amount of the ester paliperidone palmitate rather than the “mg equivalent” amount of paliperidone. Labeling the product in this manner would provide for strengths of 39 mg, 78 mg, 117 mg, 156 mg and 234 mg per syringe. (b) (4)

(b) (4)

DMEPA does not agree with the

Applicant's rationale. Using the term 'mg equivalent' is confusing and can lead to incorrect dosage calculations and conversions. Postmarketing experience with other products that express doses/strengths in terms of "equivalents" (e.g., Fosphenytoin equivalents) demonstrates such confusion. Furthermore, there is no existing data (of which FDA is aware) that any particular 'even' strengths, are 'more identifiable' than other strengths. Thus, we additionally do not agree with the Applicant's rationale to (b) (4)

In a meeting with the Division of Psychiatry Products, Office of New Quality Drug Chemistry, the Division of Medication Error Prevention and Analysis and the Chair of the CDER Labeling and Nomenclature Committee (LNC) on June 8, 2009, the team discussed the Applicant's proposal and the differences of opinion as to the preferred expression of strength. ONDQA wanted the strength expressed in terms of the ester and clinical liked the whole numbers. DMEPA did not have a preference as to how the strength was expressed but did request that whichever method was chosen, the container, carton and insert all needed to be consistent.

Following discussion the group agreed that the product strength should be expressed as the ester (paliperidone palmitate) on the container labels, carton and throughout the insert labeling. It was agreed that the syringe strengths should be labeled as 39 mg, 78 mg, 117 mg, 156 mg, and 234 mg of paliperidone palmitate, and not as 25 mg, 50 mg, 75 mg, 100 mg, or 50 mg of paliperidone. Additionally, there should not be any references to milligram equivalents, or paliperidone equivalents, or any similar terms throughout the labels and labeling, other than in the Description section of the Insert Labeling. (b) (4)

5 RECOMMENDATIONS

Our evaluation noted areas of needed improvement on the container labels, carton and insert labeling. We noted the use of the inappropriate dosage form, (b) (4) and provide comments on the insert labeling in Section 5.1 *Comments on the Division*. Section 5.2, *Comments to the Applicant*, contains our recommendations for the container labels and carton labeling. We request the recommendations in Section 5.2 be communicated to the Applicant prior to approval.

Please copy the Division of Medication Error Prevention and Analysis on any communications to the Applicant with regard to this review. If you have any further questions or need clarification on this review, please contact Abolade Adeolu, OSE Project Manager, at 301-796-4264.

5.1 COMMENTS TO THE DIVISION

1. The Applicant used the term (b) (4) throughout the labels and labeling to describe the dosage form of the proposed product throughout the labels and labeling. We note this is not an official U.S. Pharmacopeia (USP) dosage form. The chemistry review also noted this inappropriate dosage form statement. ONDQA recommended that the Applicant to replace the term "(b) (4) with the term "Extended-release Injectable Suspension" to appropriately reflect the proposed dosage form. We concur with this recommendation.

2. The syringe strengths should be referred to as 39 mg, 78 mg, 117 mg, 156 mg, and

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