CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-304

MEDICAL REVIEW(S)

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FDA CENTER FOR DRUG EVALUATION AND RESEARCH
DIVISION OF ANALGESIA, ANESTHESIA, AND RHEUMATOLOGY PRODUCTS
10903 NEW HAMPSHIRE AVENUE, BLDG 22, SILVER SPRING, MARYLAND 20993

Memorandum: Labeling Addendum

DATE: November 20, 2008

RE: Labeling addendum

NDA: 22-304
Tapentadol

THROUGH: Sharon Hertz, M.D., Deputy Directory, DAARP

FROM: Robert Shibuya, M.D., Medical Team Leader, DAARP
Ellen Fields, M.D., MPH, Medical Team Leader, DAARP

This memorandum will summarize the resolution of three labeling issues for NDA 22-304, tapentadol tablets.

1. Serotonin syndrome
   The clinical trial database was searched for the term "serotonin syndrome" and sign/symptom complexes suspicious for serotonin syndrome, and no cases were identified. The pharmacology of tapentadol reflects primarily selective norephinephrine reuptake inhibition and mu opioid agonism, however there is serotonin reuptake inhibition as well, albeit to a lesser extent. Taken in concert with the potential level of morbidity and mortality associated with serotonin syndrome, we felt that appropriate language regarding serotonin syndrome should be placed into the Warnings and Precautions section of the labeling.

2. Contraindication for concomitant use of monoamine oxidase inhibitors
   Although patients receiving MAOIs were not included in the clinical trials of tapentadol, because of the pharmacology of tapentadol and the applicant's concerns about this risk, this contraindication was included in the product labeling.

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3. Medication Guide
In their review of the abuse liability data, the Controlled Substance Staff noted that studies with tapentadol had findings consistent with a very high abuse liability (similar to hydromorphone). Despite the fact that tapentadol is likely to be classified in Schedule II by the Drug Enforcement Administration, additional patient education is considered prudent and necessary to mitigate abuse. Hence, a Medication Guide (and subsequently a REMS) has been added to the labeling for tapentadol.

APPEARS THIS WAY
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/s/

Robert Shibuya
11/20/2008 01:36:24 PM
MEDICAL OFFICER

Ellen Fields
11/20/2008 05:25:20 PM
MEDICAL OFFICER

Ellen Fields
11/20/2008 05:25:47 PM
MEDICAL OFFICER

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CLINICAL REVIEW N 22-304 Tapentadol

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Anesthesia, Analgesia and Rheumatology Products, HFD-170
10903 New Hampshire Avenue, Silver Spring, MD 20993

Medical Officer Review

Date of Submission:	**January 23, 2008**
Type of Submission:	**New Drug Application**
Product:	**Tapentadol ™**
Sponsor:	**Johnson & Johnson**
Review Date:	**September 18, 2008**
PDUFA Date:	**November 23, 2008**
Reviewer:	**Ellen W. Fields, M.D., M.P.H.** **Clinical Team Leader**
Project Manager:	**Matthew Sullivan**

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