CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-192

CHEMISTRY REVIEW(S)

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: 9 January 2009

FROM: Donghao (Robert) Lu, Ph.D.
Division of Pre-Marketing Assessment - I
Office of New Drug Quality Assessment

TO: File NDA 22-192

SUBJECT: Amendments to Pending Application (Nov. 5 and Nov. 19, 2008)

RECOMMENDATION: The drug product Iloperidone immediate-release tablets, 1, 2, 4, 6, 8, 10, and 12 mg, is recommended as APPROVAL from a CMC perspective.

ACTION: These two CMC comments have been sent to the sponsor:

(1) The text "Protect from light and moisture" should be displayed on the draft bottle labels, carton labels, blister card labels and blister card carton labels.

(2) In the labeling text (package insert), the statement [redacted] ' should be changed to "Each round, uncoated tablet contains 1 mg, 2 mg, 4 mg, 6 mg, 8 mg, 10 mg, or 12 mg of iloperidone". b(4)

REVIEW NOTE:

Vanda submitted a Complete Response on November 5, 2008 to the Agency's action letter (July 25, 2008) and a request for reconsideration of proprietary name for iloperidone on November 19, 2008. For the original NDA 22-192, the drug product Iloperidone immediate-release tablets, 1, 2, 4, 6, 8, 10, and 12 mg, was recommended as APPROVAL from a CMC perspective. The amendments provided additional information on labeling, which has some modifications and is reviewed as shown below.

4 Page(s) Withheld

_____ Trade Secret / Confidential (b4)

X Draft Labeling (b4)

X Draft Labeling (b5)

_____ Deliberative Process (b5)

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/s/

Donghao Lu
1/12/2009 03:27:42 PM
CHEMIST

Ramesh Sood
1/12/2009 03:39:44 PM
CHEMIST

Fanapta™
(iloperidone)
Tablets

NDA 22-192

Division Director Review
Chemistry, Manufacturing, and Controls

Applicant: Vanda Pharmaceuticals, Inc.
9605 Medical Center Drive, Suite 300
Rockville, MD 20850

Indication: Treatment of schizophrenia

Presentation: Immediate release, white, round, uncoated tablets are available in seven strengths (1 mg, 2 mg, 4 mg, 6 mg, 8 mg, 10 mg, and 12 mg) debossed with Vanda logo on one side and tablet strength on the other side.

Tablets of all strengths are packaged in 60 count, child-resistant, [redacted] bottles, wit[redacted], and in 2 count aluminum foil blisters on [redacted] for dose titration. Except for 1 mg and 2 mg strengths, tablets are provided in [redacted]. b(4)

EER Status: Acceptable 11-JAN-2008

Consults: EA – Categorical exclusion granted under 21 CFR §25.31(a)
Methods Validation – Revalidation by Agency not requested.

Original Submission: 27-SEP-2007

Post-Approval Agreements: None

Drug Substance:

Iloperidone is a psychotropic agent belonging to the chemical class of piperidinylbenzisoxazole derivatives. The drug substance, iloperidone , is a small, synthetic, New Molecular Entity (NME) with an empirical formula of $C_{24}H_{27}N_2O_4F$ and a molecular weight of 426.5. Known chemically as 1-[4-[3-[4-(6-fluoro-1,2-benzisoxazol-3- yl)-1-piperidinyl]propoxy]-3-methoxyphenyl] ethanone, it forms white to off-white, crystals with a melting range of 120.0-125.0°C. Iloperidone is practically insoluble in water (0.012 mg/mL), sparingly soluble in basic aqueous solutions, slightly soluble in acidic aqueous solutions, and freely soluble in chloroform, ethanol,

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