

**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

_____ ' 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)

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/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, _____ bottles, wit: _____, and in 2 count aluminum foil blisters on _____ for dose titration. Except for 1 mg and 2 mg strengths, tablets are provided in _____

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,

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.