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RESEARCH**

APPLICATION NUMBER:

22-192

APPROVAL LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-192

NDA APPROVAL

Vanda Pharmaceuticals
Attention: John Feeney, M.D.
Acting Chief Medical Officer
9605 Medical Center Drive
Suite 300
Rockville, MD 20850

Dear Dr. Feeney:

Please refer to your new drug application (NDA) dated and received September 27, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Fanapt (iloperidone) 1, 2, 4, 6, 8, 10, and 12 mg tablets.

We acknowledge receipt of your submissions and communications dated November 6, 2008, November 19, 2008, January 9, 2009, March 10, 2009, March 17, 2009, April 15, 2009, and April 24, 2009.

Your submission of November 6, 2008 constituted a complete response to our July 25, 2008 action letter.

This new drug application provides for the use of Fanapt (iloperidone) for the acute treatment of schizophrenia in adults.

We have completed our review of this application. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at <http://www.fda.gov/oc/datacouncil/spl.html> that is identical to the enclosed agreed-upon labeling text. Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission "SPL for approved NDA 22-192."

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005)*. For administrative purposes, designate this submission **“Final Printed Carton and Container Labels for approved NDA 22-192”** Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

PROPRIETARY NAME

The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Psychiatry Products do not object to the use of the proprietary name, Fanapt, for this product.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages 0 to 12 years because necessary studies are highly impractical due to the very low incidence of schizophrenia diagnosed prior to age 13.

We are deferring submission of your pediatric studies for ages 13 to 17 years for this application because the drug is ready for approval in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required by section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

1. A deferred pediatric study under PREA for the treatment of schizophrenia in pediatric patients ages 13 to 17. A study to obtain pharmacokinetic data and provide information pertinent to dosing of iloperidone tablets in the relevant pediatric population.

Final Protocol Submission:	by March 1, 2010
Study Completion Date:	by September 1, 2013
Final Report Submission:	by March 1, 2014

2. A deferred pediatric study under PREA for the treatment of schizophrenia in pediatric patients ages 13 to 17. A study of the efficacy and safety of iloperidone tablets in the relevant pediatric population.

Final Protocol Submission:	by March 1, 2010
Study Completion Date:	by September 1, 2013
Final Report Submission:	by March 1, 2014

Submit final reports to this NDA. Use the following designator to prominently label all submissions:

Required Pediatric Assessment(s)

POSTMARKETING REQUIREMENTS UNDER 505(o)

Section 505(o) of the Federal Food Drug and Cosmetic Act (FDCA) authorizes FDA to require holders of approved drug and biological product applications to conduct postmarketing studies and clinical trials for certain purposes, if FDA makes certain findings required by the statute (section 505(o)(3)(A)).

We have determined that an analysis of spontaneous postmarketing adverse events reported under subsection 505(k)(1) of the FDCA will not be sufficient to assess a signal of a serious risk of carcinogenicity and to identify an unexpected serious risk of drug interactions.

Furthermore, the new pharmacovigilance system that FDA is required to establish under section 505(k)(3) of the FDCA has not yet been established and is not sufficient to assess these serious risks.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following studies:

3. Complete the ongoing P95 carcinogenicity study.

The timetable you submitted on April 24, 2009 states that you will conduct this study according to the following timetable:

Study Completion Date:	by February 28, 2010
Final Report Submission:	by May 31, 2010

4. Conduct a study investigating the possible in vitro interaction of iloperidone and P-Glycoprotein (P-Gp).

The timetable you submitted on April 15, 2009 states that you will conduct this study according to the following timetable:

Final Protocol Submission:	by August 1, 2009
Study Completion Date:	by October 1, 2009
Final Report Submission:	by November 1, 2009

Finally, we have determined that only a clinical trial (rather than a nonclinical or observational study) will be sufficient to identify an unexpected serious risk of Fanapt (iloperidone) to patients with hepatic dysfunction.

Therefore, based on appropriate scientific data, FDA has determined that you are required to conduct the following clinical trial:

5. A repeat of your clinical trial CIL0522A0103, conducted with a group of subjects with mildly and moderately impaired hepatic function, comparing them to normals in the same trial.

The timetable you submitted on April 15, 2009 states that you will conduct this trial according to the following timetable:

Final Protocol Submission:	by November 1, 2009
Trial Completion Date:	by November 1, 2010
Final Report Submission:	by May 1, 2011

Submit clinical protocols to your IND for this product, with a cross-reference letter to this NDA. Submit all final reports to your NDA. Prominently identify the submissions with the following wording in bold capital letters at the top of the first page of the submission, as appropriate:

REQUIRED POSTMARKETING PROTOCOL under 505(o)
REQUIRED POSTMARKETING FINAL REPORT under 505(o)
REQUIRED POSTMARKETING CORRESPONDENCE under 505(o)

Section 505(o)(3)(E)(ii) of the FDCA requires you to report periodically on the status of any study or clinical trial required under this section. This section also requires you to periodically report to FDA on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Section 506B of the FDCA, as well as 21 CFR 314.81(b)(2)(vii) requires you to report annually on the status of any postmarketing commitments or required studies or clinical trials.

FDA will consider the submission of your annual report under section 506B and 21 CFR 314.81(b)(2)(vii) to satisfy the periodic reporting requirement under section 505(o)(3)(E)(ii) provided that you include the elements listed in 505(o) and 21 CFR 314.81(b)(2)(vii). We remind you that to comply with 505(o), your annual report must also include a report on the status of any study or clinical trial otherwise undertaken to investigate a safety issue. Failure to submit an annual report for studies or clinical trial required under 505(o) on the date required will be considered a violation of FDCA section 505(o)(3)(E)(ii) and could result in enforcement action.

POSTMARKETING COMMITMENTS

We remind you of the following postmarketing commitment agreed upon in our communication dated April 15, 2009:

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.