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RESEARCH**

APPLICATION NUMBER:
202100Orig1s000

OTHER ACTION LETTER(s)



NDA 202100

COMPLETE RESPONSE

NextWave Pharmaceuticals, Inc.
Attention: Michael Burdick
VP, Product Development
20450 Stevens Creek Blvd, Suite 150
Cupertino, CA 95014

Dear Mr. Burdick:

Please refer to your New Drug Application (NDA) dated July 29, 2010, received July 30, 2010, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for QUILLIVANT (methylphenidate hydrochloride) for extended-release oral suspension.

We acknowledge receipt of your amendments dated:

| | | |
|-------------------|----------------|-----------------|
| August 18, 2010 | March 7, 2011 | May 16, 2011 |
| November 23, 2010 | March 17, 2011 | May 19, 2011 |
| December 16, 2010 | March 31, 2011 | August 24, 2011 |
| January 11, 2011 | April 15, 2011 | August 29, 2011 |
| January 25, 2011 | April 22, 2011 | |
| February 7, 2011 | May 5, 2011 | |

We have completed our review of this application, as amended, and have determined that we cannot approve this application in its present form. We have described our reasons for this action below and, where possible, our recommendations to address these issues.

FACILITY INSPECTIONS

During a recent inspection of the Tris Pharma, Inc. manufacturing facility for this application, our field investigator conveyed deficiencies to the representative of the facility. Satisfactory resolution of these deficiencies is required before this application may be approved.

ADDITIONAL COMMENTS

CLINICAL PHARMACOLOGY

The Office of Clinical Pharmacology has determined that the reassayed sample data submitted provide sufficient evidence for the reliability of the original bioanalytical data and PK results, based on the following:

1. The efficacy study (NWP06-ADD-100) clearly demonstrated the efficacy of the product in pediatric patients. This renders the PK information supportive.
2. Overall, about 200 samples were reassayed, and the retested concentrations on average were within 3-17% of the original concentration values based on linear regression analysis. For study NWP06-PPK-101, the retested concentrations for 27 out of the 29 samples were within 20% of the original values. For study S09-0238, the retested concentrations for 98 out of the 166 samples were within 20% of the original values.
3. The clinical response in the Qullivant arm was superior to placebo between 45 min and 11.5 hrs post-dosing, indicating adequate drug concentrations between those times. The drug concentrations for Qullivant product are in the range of concentrations observed for other products with similar clinical response profiles (e.g. methylin IR, Concerta) particularly at the early and late time points.
4. PK parameters for Methylin IR oral solution which was used as the RLD in this application were compared to those from the original NDA 21419. Mean AUC and Cmax values for methylphenidate are quite comparable between NDA 21419 and the current submission. This provides additional evidence for the reliability of the data submitted for this NDA.

LABELING

- We reserve comment on the proposed labeling until the application is otherwise adequate. If you revise labeling, your response must include updated content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>.

OTHER

Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 314.110. If you do not take one of these actions, we may consider your lack of response a request to withdraw the application under 21 CFR 314.65. You may also request an extension of time in which to resubmit the application. A resubmission must fully address all the deficiencies listed. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.

Under 21 CFR 314.102(d), you may request a meeting or telephone conference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the FDA's "Guidance for Industry - Formal Meetings Between the FDA and Sponsors or Applicants," May 2009 at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM153222.pdf>.

The drug product may not be legally marketed until you have been notified in writing that this application is approved.

If you have any questions, call Shin-Ye Sandy Chang, Regulatory Project Manager, at (301) 796-3971.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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

/s/

THOMAS P LAUGHREN
08/30/2011