DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022331/S-001/S-002

SUPPLEMENT APPROVAL

Shionogi Pharma, Inc.
Attention: Allison Lowry, RAC
Director, Regulatory Affairs
Five Concourse Parkway, Suite 1800
Atlanta, GA 30328

Dear Ms. Lowry:

Please refer to your Supplemental New Drug Applications (sNDAs) dated September 29, 2009, received September 30, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Kapvay (clonidine hydrochloride) extended-release tablets, 0.1 mg and 0.2 mg.

We acknowledge receipt of your amendments dated August 5, 2010, and September 7, 2010.

The August 5, 2010, submission constituted a complete response to our July 28, 2010, action letter.

These "Prior Approval" supplemental new drug applications provide for the use of Kapvay (clonidine hydrochloride) extended-release tablets for the treatment of attention deficit hyperactivity disorder (ADHD) as monotherapy (S-001) or as adjunctive therapy to stimulant medications (S-002).

We have completed our review of these applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed 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, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the package insert, text for the patient package insert). Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the carton and immediate container labels submitted on August 5, 2010, 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 (June 2008)." Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "Final Printed Carton and Container Labels for approved NDA 022331/S-001/S-002." Approval of this submission by FDA is not required before the labeling is used.

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, Kapvay, 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 5 years of age because the product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this age group **and** is not likely to be used in a substantial number of pediatric patients in this group.

- The diagnostic criteria and assessment measures for determining efficacy for the treatment of ADHD in children less than 6 years old are not well defined.
- Pharmaceutical treatment in this age group is uncommon.
- Kapvay is a solid dose, extended-release formulation, available in 0.1 mg and 0.2 mg strengths, and its tablets cannot be subdivided. Since a liquid/rapid-melt form and additional strengths are not available, it is not expected that the product will be prescribed for potential ADHD patients less than 6 years old.

We are deferring submission of the additional pediatric studies for ages 6 to 17 for this application because pediatric studies should be delayed until additional safety or effectiveness data have been collected.

A longer-term randomized withdrawal maintenance study of efficacy and safety of clonidine hydrochloride extended-release tablets as monotherapy, or alternatively, as adjunctive therapy, in children and adolescents is required because ADHD is a chronic condition and it is very likely that most patients who respond in short term treatment will be extended for longer-term treatment.

Additionally, a juvenile animal study of clonidine in combination with a stimulant as a postmarketing requirement (as communicated in the minutes of our 3/9/09 meeting) is required.

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.

1676-1 Deferred pediatric study under PREA for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) in pediatric patients ages 6 to 17: A longer-term randomized withdrawal maintenance study of efficacy and safety of clonidine hydrochloride extended-release tablets as monotherapy, or alternatively, as adjunctive therapy, in children and adolescents

Final Protocol Submission:	April 2011
Study Initiation:	August 2011
Final Report Submission:	December 2013

1676-2 Juvenile animal study:
In order to support safe use of clonidine in combination with stimulants in pediatric patients and to provide additional safety information for labeling, you must conduct a juvenile animal study of clonidine in combination with a stimulant as a postmarketing requirement (as communicated in the minutes of our 3/9/2009 meeting).

Final Protocol Submission:	10/31/2011
Study Initiation:	01/30/2012
Final Report Submission:	04/30/2013

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/opacom/morechoices/fdaforms/cder.html; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA, to CDERMedWatchSafetyAlerts@fda.hhs.gov, and to the following address:

MedWatch Program
Office of Special Health Issues
Food and Drug Administration
10903 New Hampshire Ave
Building 32, Mail Stop 5353
Silver Spring, MD 20993

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Hiren D. Patel, Pharm.D., Regulatory Project Manager, at (301) 796-2087.

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

ENCLOSURE:
Content of Labeling

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
09/28/2010