DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022499
NDA 022500

NDA APPROVAL

Tris Pharma, Inc.
Attention: W. Scott Groner
Director Regulatory Affairs and Compliance
2033 Route 130, Suite D
Monmouth Junction, NJ 08502

Dear Mr. Groner:

Please refer to your January 13, 2009 new drug application (NDA 022499), received on February 3, 2009 (User Fee receipt date), submitted under section 505(b)(2) of the Federal Food, Drug and Cosmetic Act for Clonidine Extended-Release (ER) Oral Suspension, 0.09 mg/mL.

Please, also refer to your January 13, 2009 new drug application (NDA 022500), received on February 3, 2009 (User Fee receipt date), submitted under section 505(b)(2) of the Federal Food, Drug and Cosmetic Act for Clonidine Extended-Release (ER) 0.17 mg and 0.26 mg Tablets.

We acknowledge receipt of your submissions dated March 6, 9, 23, 27, April 8, June 5, 24, July 10, 23, August 7, 17, 25, 26, September 4, 25, October 8, 27 and November 3, 16, 18, 24, 25, 2009.

These new drug applications provide for the use of Clonidine ER Oral Suspension (NDA 022499) and Clonidine ER Tablets (NDA 022500) for the treatment of hypertension.

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.

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 labeling (text for the package insert). 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 022499 and SPL for approved NDA 022500**." Approval of this submission by FDA is not required before the labeling is used.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the submitted carton and immediate 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)*. 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 022499 and Final Printed Carton and Container Labels for approved NDA 022500**." Approval of this submission by FDA is not required before the labeling is used.

Marketing these products with FPL that is not identical to the approved labeling text may render these products misbranded and unapproved new drugs.

PROPRIETARY NAME

If you choose to use a proprietary name for these products, the name and its use in the labels must conform to the specifications under 21 CFR 201.10 and 201.15. Please submit any proprietary name to the Agency for our review prior to its implementation.

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.

For NDA 022500, we are waiving the pediatric study requirement for this application because the efficacy and safety information will be provided by the pediatric studies to be conducted under NDA 022499 (Clonidine (ER) oral suspension).

For NDA 022499:

We are waiving the pediatric study requirement for ages 0 to <1 year because necessary studies are impossible or highly impracticable. This is because the number of pediatric patients with hypertension is small.

We are deferring submission of your pediatric study for ages 1 to ≤18 years (b) (4)

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

1. Deferred pediatric study under PREA for the treatment of hypertension in pediatric patients ages 1 to ≤18.

   Protocol Submission: December 3, 2010
   Final Report Submission: December 3, 2011

Submit final study reports to this NDA. For administrative purposes, all submissions related to this required pediatric postmarketing study must be clearly designated "**Required Pediatric Assessment**".

POSTMARKETING COMMITMENTS

We remind you of your postmarketing study commitment, agreed to in your email dated December 1, 2009. This commitment is listed below.

Description of Commitment: You will perform a "Thorough QT Study" as described in ICH E14. This study can utilize your extended release formulation or an immediate-release formulation. It can utilize a single 0.6-mg dose group and a single administration.

Protocol Submission: by December 3, 2010
Final Report Submission: by December 3, 2011

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments should be prominently labeled "**Postmarketing Study Commitment Protocol**," "**Postmarketing Study Commitment Final Report**," or "**Postmarketing Study Commitment Correspondence**."

PROMOTIONAL MATERIALS

In addition, we request that you submit one copy of the introductory promotional materials you propose to use for these products to this division.

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important safety-related information about these drug products (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to the appropriate this NDA and to the following address:

MedWatch
Food and Drug Administration
Suite 12B-05
5600 Fishers Lane
Rockville, MD 20857

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, please call Mr. Devi Kozeli, RAC., Regulatory Project Manager, at (301) 796-1128.

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure: Agreed-upon labeling text and container labels.