DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22499/S-001
NDA 22500/S-001

SUPPLEMENT 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 Supplemental New Drug Application (sNDA) dated January 25, 2010, received January 26, 2010, submitted under section 505(b)/pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Nexiclon XR Extended-Release 0.09 mg/mL Oral Suspension (NDA 22499).

We also refer to your Supplemental New Drug Application (sNDA) dated January 25, 2010, received January 26, 2010, submitted under section 505(b)/pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Nexiclon XR Extended-Release 0.17 mg and 0.26 mg Tablets (NDA 22500).

We acknowledge receipt of your amendments dated August 11, 2010.

These "Prior Approval" supplemental new drug applications provide for labeling revised as follows:

1. The abbreviation "ER" has been replaced throughout the labeling with 'Extended-Release'.

2. The Clonidine Hydrochloride equivalency to Nexiclon XR information has been removed throughout the labeling.

3. For the oral suspension labeling, under DOSAGE AND ADMINISTRATION the following paragraph has been added:

2.3 Patients Currently Using Clonidine Hydrochloride Immediate-Release Tablets

The recommended dose of NEXICLON XR for patients who are currently taking clonidine hydrochloride immediate-release tablets is provided in the table below.

	NEXICLON XR (clonidine) Extended-Release Oral Suspension	**Equivalent dose of Clonidine HCl Immediate-Release Tablets**
Initial Dose	0.17 mg (2 mL) once daily	0.1 mg twice daily
Maintenance Dose Titration Increments	0.09 mg (1 mL) once daily	0.05 mg twice daily
Common Doses Used for Blood Pressure Effect	0.17 mg (2 mL) once daily	0.1 mg twice daily
	0.34 mg (4 mL) once daily	0.2 mg twice daily
	0.52 mg (6 mL) once daily	0.3 mg twice daily

4. For the tablet labeling under DOSAGE AND ADMINISTRATION the following paragraph was added:

2.3 Patients Currently Using Clonidine Hydrochloride Immediate-Release Tablets

The recommended dose of NEXICLON XR for patients who are currently taking clonidine hydrochloride immediate-release tablets is provided in the table below.

	NEXICLON XR (clonidine) Extended-Release Tablets	**Equivalent dose of Clonidine HCl Immediate-Release Tablets**
Initial Dose	0.17 mg once daily	0.1 mg twice daily
Maintenance Dose Titration Increments	0.09 mg once daily	0.05 mg twice daily
Common Doses Used for Blood Pressure Effect	0.17 mg once daily	0.1 mg twice daily
	0.34 mg once daily	0.2 mg twice daily
	0.52 mg once daily	0.3 mg twice daily

5. The font size of the strengths on the principal display panel of the 0.09 mg/mL oral suspension label and carton labeling, and the 0.17 mg and 0.26 mg on the container labels was increased in order to minimize the potential for wrong dose medication errors during order processing, dispensing and drug administration.

We have completed our review of these supplemental applications, as amended. They are approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling.

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**."

For **NDA 022499**, we remind you of your postmarketing study requirement. This requirement 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, 2011
   Final Report Submission: December 3, 2012

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**".

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 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.

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

/s/

NORMAN L STOCKBRIDGE
09/23/2010