DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 022382 **NDA APPROVAL**

Roxro Pharma, Inc.
535 Middlefield Road
Suite 180
Menlo Park, CA 94025

Attention: Roger Whiting, PhD
President and Chief Scientific Officer

Dear Dr. Whiting:

Please refer to your new drug application (NDA) dated December 5, 2008, received December 5, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for Sprix™ (ketorolac tromethamine) Nasal Spray.

We acknowledge receipt of your amendments dated December 12, 2008, and January 8, 13, and 28, February 5, 16, and 27, April 29, May 4(2) and 20, June 12, 23, and 29, July 1, 3, and 17, August 4, 13, 20, and 24, September 3, 25, and 28, November 19, 2009, and April 18, 2010.

The November 19, 2009 submission constituted a complete response to our October 5, 2009 action letter.

This new drug application provides for the use of Sprix™ (ketorolac tromethamine) Nasal Spray for short term (up to 5 days) management of moderate to severe pain that requires analgesia at the opioid level.

We have completed our review of this application, as amended. It is 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, 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, Medication Guide). 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.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the carton and immediate container labels submitted on April 18, 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 (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 022382**." 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.

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 in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are deferring submission of your pediatric studies for ages 0 to 17 years until December 2013, because pediatric studies should be delayed until additional safety or effectiveness data have been collected. These pediatric studies are expected to generate important information regarding the dosing, efficacy, and safety of the ketorolac moiety in the pediatric population. Furthermore, because of the new route of administration, it will be important to determine whether the Sprix (ketorolac tromethamine) formulation poses any specific safety issues in the pediatric population.

Your deferred pediatric studies required under 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.

1551-1. Deferred pediatric study under PREA for the short term (up to 5 days) management of moderate to severe pain that requires analgesia at the opioid level in pediatric patients ages 0 to 17 years.

Protocol Submission:	October 2011
Study Start:	December 2012
Final Report Submission:	December 2013

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(s)**".

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

In our email dated September 28, 2009, we notified you that a risk evaluation and mitigation strategy (REMS) was required for Sprix (ketorolac tromethamine) Nasal Spray to ensure that the benefits of the drug outweigh the risks of cardiovascular and gastrointestinal adverse events. We indicated that your REMS must include a Medication Guide and a timetable for submission of assessments of the REMS.

After consultations between the Office of New Drugs and the Office of Surveillance and Epidemiology, we have reconsidered the need for a REMS for this product. We believe that a Medication Guide is necessary to inform patients of the serious risks of cardiovascular and gastrointestinal adverse events. However, since other drugs currently approved in the nonsteroidal anti-inflammatory drug (NSAID) class have Medication Guides with identical safety information regarding these risks that are not included in a REMS, we will not require a REMS.

PROMOTIONAL MATERIALS

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

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see 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.

EXPIRATION DATING PERIOD

An expiry of 24 months is granted under the recommended storage conditions: Store at 2°- 8°C (36^{o}- 46^{o} F). An in-use period of one day at ambient conditions is allowed.

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
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, call Jessica Benjamin, Regulatory Project Manager, at (301) 796-3924.

Sincerely,

{See appended electronic signature page}

Sharon Hertz, M.D.
Deputy Director
Division of Anesthesia and Analgesia Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosures: Package Insert
Medication Guide
Carton and Immediate Container Labeling

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22382	ORIG-1	ROXRO PHARMA INC	Sprix (ketorolac tromethamine) nasal spray

---

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

/s/

SHARON H HERTZ
05/14/2010