DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 22-202

NDA APPROVAL

Xanodyne Pharmaceuticals, Inc.
One Riverfront Place
Newport, KY 41071-4563

Attention: Arthur C. Ilse
Director, Regulatory Affairs

Dear Mr. Ilse:

Please refer to your new drug application (NDA) dated September 21, 2007, received September 21, 2007, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Zipsor (diclofenac potassium) Liquid Filled Capsules.

We acknowledge receipt of your submissions dated January 23, March 24, April 10, April 18, July 25, and December 16, 2008 and March 18, March 26, May 19, June 2, June 11, and June 12, 2009.

The December 16, 2008 submission constituted a complete response to our July 21, 2008 action letter.

This new drug application provides for the use of Zipsor (diclofenac potassium) Liquid Filled Capsules for relief of mild to moderate pain.

We have completed our review of this application, as amended, and it is 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, 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 and medication guide). 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 22-202**."

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the enclosed blister cards, 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 22-202**." 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(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages birth to 1 year because there is evidence strongly suggesting that the drug product would be ineffective and unsafe in this pediatric group. Pharmacokinetic pathways for the drug metabolism are not fully developed at this age.

We are deferring submission of your pediatric studies for ages 1to 17 years for this application because this product is ready for approval for use in adults and the pediatric studies have not been completed.

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.

1. Deferred pediatric study under PREA for the treatment of relief of mild to moderate acute pain in pediatric patients ages ≥12 to 17 years.

Final Protocol Submission Date:	January 19, 2010
Study Start Date:	July 16, 2010
Final Report Submission:	July 16, 2012

2. Deferred pediatric study under PREA for the treatment of relief of mild to moderate acute pain in pediatric patients ages ≥ 2 to 12 years.

Final Protocol Submission Date:	July 16, 2012
Study Start Date:	January 16, 2013
Final Report Submission:	January 16, 2015

3. Deferred pediatric study under PREA for the treatment of relief of mild to moderate acute pain in pediatric patients ages ≥ 1 to 2 years.

Final Protocol Submission Date:	January 16, 2015
Study Start Date:	July 16, 2015
Final Report Submission:	July 17, 2017

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

RISK EVALUATION AND MITIGATION STRATEGY REQUIREMENTS

Section 505-1 of the Federal Food, Drug, and Cosmetic Act (FDCA) authorizes FDA to require the submission of a Risk Evaluation and Mitigation Strategy (REMS) if FDA determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)).

In accordance with section 505-1 of FDCA, as one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR Part 208. Pursuant to 21 CFR Part 208, FDA has determined that Zipsor (diclofenac potassium) Liquid Filled Capsules pose a serious and significant public health concern requiring the distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of Zipsor (diclofenac potassium) Liquid Filled Capsules. FDA has determined that Zipsor (diclofenac potassium) Liquid Filled Capsules is a product for which patient labeling could help prevent serious adverse effects and has serious risks (relative to benefits) of which patients should be made aware because information concerning the risks could affect patients' decisions to use, or continue to use Zipsor (diclofenac potassium) Liquid Filled Capsules.

Under 21 CFR 208, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed Zipsor (diclofenac potassium) Liquid Filled Capsules.

Your proposed REMS, submitted on June 11, 2009, and appended to this letter, is approved. The REMS consists of the Medication Guide included with this letter and the timetable for submission of assessments of the REMS.

Your assessment of the REMS should include an evaluation of:

a. Patients' understanding of the serious risks of Zipsor (diclofenac potassium) Liquid Filled Capsules
b. A report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24
c. A report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance

You should submit the final methodology and content of the patient survey at least 90 days prior to initiating the conduct of the survey.

The requirements for assessments of an approved REMS under section 505-1(g)(3) include, in section 505-1(g)(3)(B) and (C), requirements for information on the status of any postapproval study or clinical trial required under section 505(o) or otherwise undertaken to investigate a safety issue. You can satisfy these requirements in your REMS assessments by referring to relevant information included in the most recent annual report required under section 506B and 21 CFR 314.81(b)(2)(vii) and including any updates to the status information since the annual report was prepared. Failure to comply with the REMS assessments provisions in 505-1(g) could result in enforcement action.

We remind you that in addition to the assessments submitted according to the timetable included in the approved REMS, you must submit a REMS assessment and may propose a modification to the approved REMS when you submit a supplemental application for a new indication for use as described in Section 505-1(g)(2)(A) of the FDCA.

Prominently identify submissions containing REMS assessments or proposed modifications of the REMS with the following wording in bold capital letters at the top of the first page of the submission:

NDA 22-202 REMS ASSESSMENT

NEW SUPPLEMENT FOR NDA 22-202
PROPOSED REMS MODIFICATION
REMS ASSESSMENT

NEW SUPPLEMENT FOR (NEW INDICATION FOR USE)
FOR NDA 22-202
REMS ASSESSMENT

NDA 22-202 PROPOSED REMS MODIFICATION (if included)

If you do not submit electronically, please send 5 copies of REMS-related submissions.

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(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

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), 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 www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

EXPIRATION DATING PERIOD

An expiration dating period of 30 months is granted to the Zipsor Liquid Filled Capsules in HDPE bottles, stored at 25ºC/60%RH. An expiry period of 15 months is granted for Zipsor Liquid Filled capsules in blisters, stored at 25 ºC/60%RH.

LETTERS TO HEALTH CARE PROFESSIONALS

If you 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 an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
Suite 12B05
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 Tanya Clayton, Regulatory Project Manager, at (301) 796-0871.

Sincerely,

{See appended electronic signature page}

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

Enclosure: Package Insert
Medication Guide
Carton and Immediate Container Labeling
REMS

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

/s/

Sharon Hertz

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