**DEPARTMENT OF HEALTH & HUMAN SERVICES** Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 8-107/S-054

Xanodyne Pharmacal, Inc.
Attention: Keith Moore, Pharm.D.
Sr. Director, Products and Medical Affairs
7310 Turfway Road
Suite 490
Florence, KY 41042

Dear Dr. Moore:

Please refer to your supplemental new drug application dated October 27, 2000, received October 30,2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Leucovorin Calcium for Injection.

We also refer to your submission dated February 22, 2001 and received on February 23, 2001.

This "Changes Being Effected" supplemental new drug application provides for labeling changes to add a Geriatric Use subsection in accordance with the CRF 201.57 (f) (10) (ii) (c) and (iii) (B) and for an added paragraph regarding pharmacokinetics in the Clinical Pharmacology section. These regulations provide language for labeling if the clinical studies provide evidence that elderly patients require specific monitoring or dosage adjustment and if the drug is found to be excreted by the kidneys.

We have completed the review of this supplemental application and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, the supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted on October 27, 2000) with the revisions requested below.

1. In your proposed pharmacokinetics paragraph, please add “in healthy male subjects” at the end of the first sentence. Also, delete the footnote at end of the paragraph.

2. It is the policy of this division not to include references in the labeling of oncology drugs, except safe handling references for cytotoxic drugs. Therefore, please delete reference #1.

3. Under the DOSAGE AND ADMINISTRATION section, the last paragraph of the Advanced Colorectal Cancer subsection the following paragraph is outdated and should be deleted:

> "Several other doses and schedules of leucovorin/5-fluorouracil therapy have also been evaluated in patients with advanced colorectal cancer; some of these alternative regimens may also have efficacy in the treatment of this disease. However, further clinical research will be required to confirm the safety and effectiveness of these alternative leucovorin/5-flurouracil treatment regimens."

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 8-107/S-054." Approval of this submission by FDA is not required before the labeling is used.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please call Patty Garvey, Regulatory Project Manager, at 301-594-5766.

Sincerely,

*{See appended electronic signature page}*

Richard Pazdur, M.D.
Director
Division of Oncology Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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

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/s/

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Richard Pazdur

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