



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 15-197/S-040  
NDA 15-229/S-031  
NDA 15-230/S-031

Xanodyne Pharmaceutical, Inc.  
Attention: James Young, Ph.D.  
Vice President, Product Development & Professional Services  
7300 Turfway Road, Suite 300  
Florence, KY 41042

Dear Dr. Young:

Please refer to your supplemental new drug applications dated July 30, 2003, received July 31, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Amicar (aminocaproic acid) Tablets, Injection, and Syrup.

We acknowledge receipt of your submissions dated February 23 and August 23, 2004.

Your submission of February 23, 2004 constituted a complete response to our January 30, 2004 action letter.

These supplemental new drug applications provide for revisions to the INDICATIONS AND USAGE section as discussed with the Division of Drug Marketing, Advertising, and Communication (DDMAC) and the Division of Gastrointestinal and Coagulation Drug Products (DGCDP).

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

The final printed labeling (FPL) must be identical to the submitted labeling (package insert submitted February 23, 2004) with the agreed-upon labeling revisions listed below, which you found acceptable in your fax dated August 23, 2004.

1. As per the Pregnancy Labeling Team recommendations, in the **INDICATIONS AND USAGE** section, third sentence, the phrase "*abruptio placentae*" should be revised to read "*acute and life-threatening abruptio placentae*".

2. As per the Division of Pediatric Drug Development recommendations, the **PRECAUTIONS, Pediatric Use** section of the label should be revised to read as follows:

“Safety and effectiveness in pediatric patients have not been established.

Amicar Injection contains benzyl alcohol as a preservative. Benzyl alcohol has been associated with a fatal “gaspings syndrome” in neonates. The “gaspings syndrome”, characterized by central nervous system depression, metabolic acidosis, gasping respirations, and high levels of benzyl alcohol and its metabolites found in the blood and urine, has been associated with exposure to benzyl alcohol in neonates and low-birth weight neonates. Additional symptoms may include gradual neurological deterioration, seizures, intracranial hemorrhage, hematologic abnormalities, skin breakdown, hepatic and renal failure, hypotension, bradycardia, and cardiovascular collapse (See **WARNINGS**).”

3. At the beginning of the **WARNINGS** section add the following:

“AMICAR Injection contains benzyl alcohol as a preservative. The administration of medications containing benzyl alcohol as a preservative to premature neonates has been associated with fatal ‘Gaspings Syndrome’. (See **PRECAUTIONS, Pediatric Use**).”

Please submit the FPL electronically according to the guidance for industry titled, “Providing Regulatory Submissions in Electronic Format – NDA.” Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, these submissions should be designated “FPL for approved supplements NDA 15-197/S-040, 15-229/S-031, 15-230/S-031.” Approval of these submissions by FDA is not required before the labeling is used.

In addition, submit three copies of the introductory promotional materials that you propose to use for these products. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

NDA 15-197/S-040  
NDA 15-229/S-031  
NDA 15-230/S-031  
Page 3

If you issue a letter communicating important information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit a copy of the letter to these NDAs and a copy to the following address:

MEDWATCH, HFD-410  
FDA  
5600 Fishers Lane  
Rockville, MD 20857

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 Ryan Barraco, Consumer Safety Officer, at 301-443-8017.

Sincerely,

*{See appended electronic signature page}*

Joyce Korvick, M.D., M.P.H  
Acting Director  
Division of Gastrointestinal & Coagulation Drug  
Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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

/s/

-----  
Joyce Korvick  
8/24/04 05:14:57 PM