CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40253

ADMINISTRATIVE DOCUMENTS

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 40-253 Date of Submission: December 1, 1999

Applicant's Name: Pharmaceutical Associates, Inc.

Established Name: Ethosuximide Syrup, 250 mg/5 mL

Labeling deficiencies:

INSERT

1. DESCRIPTION

   We note that you have revised your Components and Composition Statements reflecting addition of Sodium Hydroxide for pH adjustment of your drug product. We ask that you include Sodium Hydroxide in the listing of inactive ingredients and indicate the pH range of your product.

2. HOW SUPPLIED

   You may indicate how many unit-dose cups will be packaged in the tray. (i.e., 10 cups)

Please revise your package insert labeling, as instructed above, and submit in final print.

Prior to approval, it may be necessary to further revise your labeling subsequent to approved changes for the reference listed drug. We suggest that you routinely monitor the following website for any approved changes-

http://www.fda.gov/cder/ogd/rld/labeling_review_branch.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

/S/

William Peter Rickman
Acting Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 40-253 Date of Submission: April 23, 1998

Applicant's Name: Pharmaceutical Associates, Inc.

Established Name: Ethosuximide Syrup, 250 mg/5 mL

Labeling Deficiencies:

1. UNIT DOSE TRAY LABELING:

   a. We encourage you to revise the storage temperature to be consistent with your container labels and insert labeling.

   b. We encourage the inclusion of the statement "Each 5 mL contains: Ethosuximide, 250 mg." as found on the container labels.

2. INSERT - DOSAGE AND ADMINISTRATION:

   a. First sentence:

      Ethosuximide syrup is ...

   b. Last sentence:

      The *optimal* dose... [italicized]

   Please revise your labels and labeling, as instructed above, and submit final printed labels and labeling.

   Please note that we reserve the right to request further changes in your labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

/S/

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

RECORD OF TELEPHONE CONVERSATION

I contacted the firm today to follow-up on their previous contact with John Grace regarding the labeling review for ANDA 40-253.

Kaye McDonald believes that the firm may have misplaced the review date of submission: March 26, 1997. The review was completed 7/8/97.

Kaye McDonald stated that the firm has been very busy, and that they are just now getting around to this application.

I told her that I will send a copy of the review via fax. I instructed her to the follow the directions on the chemistry cover sheet dated July 7, 1997, and that the firm should submit a response to the chemistry and labeling at the same time.

Message confirmation is attached to the Fax Cover Sheet.

X:\NEW\FIRMSNZ\PHARMACE\TELECONS\40253FEB.98

DATE
February 23, 1998

ANDA NUMBER
40-253

IND NUMBER

TELECON

INITIATED BY FDA

PRODUCT NAME
Ethosuximide Syrup, USP

FIRM NAME
Pharm Associates

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD
Kaye McDonald, Director of Scientific Affairs

TELEPHONE NUMBER
Tel: (864)277-7282
Fax: (864)277-8045

SIGNATURE

/S/

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 40-253 Date of Submission: March 26, 1997

Applicant's Name: Pharmaceutical Associates, Inc.

Established Name: Ethosuximide Syrup, 250 mg/5 mL

Labeling Deficiencies:

1. CONTAINER - 16 oz (474 mL)

   a. "NDC" or "N" should precede the 10 digit numbers at the top of your label. We refer you to 21 CFR 207.35.

   b. Wherever the established name appears the strength "250 mg/5 mL" should immediately follow.

2. CONTAINER - Unit-Dose lid

   a. Place periods after the statements "For Institutional...", "Caution: Federal..." and "Usual Dosage: See...".

   b. See comment "b" under CONTAINER 16 oz.

3. CARTON LABELS - Tray labels

   See comment "b" under CONTAINER 16 oz.

4. INSERT

   a. GENERAL COMMENT

      Please note that the currently approved labeling for the referenced listed drug, Zarontin® Syrup, manufactured by Parke Davis was approved on October 16, 1981 with a revision date of September 1981. Please make the following changes as requested below.

   b. DESCRIPTION

      Rather than using "flavor" in the listing for the inactive ingredient please cite the flavoring agent(s).

c. WARNINGS

i. Delete the second sentence "Should signs and/or...at that point.

ii. Create separate paragraphs at the following locations:

1) Ethosuximide is capable...changes...have been reported. (changes should be plural)

2) Ethosuximide should be administered ...the drug.

iii. "USAGE IN PREGNANCY" should appear in lower cases letters. In addition please make the following changes:

1) Insert the following text as the first paragraph:

The effects of ethosuximide in human pregnancy and nursing infants are unknown.

2) Second paragraph - ...e.g.,... rather than "eg.".

d. PRECAUTIONS

i. Insert a paragraph break after the first sentence and before the second subsection. Please ensure paragraph breaks occur at the appropriate locations throughout the insert.

ii. Information for Patients - Delete the second and third paragraphs. They do not appear in the latest **approved** labeling for the listed drug.

iii. Drug Interactions - Delete this subsection.

e. ADVERSE REACTIONS

i. Gastrointestinal System - Delete the last sentence "There have been reports ....tongue".

ii. Hemopoietic System - Add "aplastic anemia" after "pancytopenia,". Delete

iii. Integumentary System - Delete

iv. Delete the following subsections - Special Senses and Genitourinary System.

v. Add the following subsection:

Miscellaneous: Other reactions reported have included myopia, vaginal bleeding, swelling of the tongue, gum hypertrophy, and hirsutism.

f. DOSAGE AND ADMINISTRATION

Italicize the words "initial" and "optimal" (2 instances - first and second paragraph).

g. OVERDOSAGE

Delete this section. It does not appear in the latest approved labeling at this time.

h. HOW SUPPLIED

i. We encourage you to cite the metric equivalent of "1 pint" (474 mL) in association with the english unit.

ii. Replace "U.D." with "unit dose".

iii. Ethosuximide Syrup is supplied as:...

Please revise your labels and labeling, as instructed above, and submit final printed labels and labeling.

Please note that we reserve the right to request further changes in your labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

/S/ for / 7-21-97

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research