



DEPARTMENT OF HEALTH & HUMAN SERVICES

HFA-305

Public Health Service

Food and Drug Administration
Rockville MD 20857

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JUL - 9 2002

Pharmaceutical Associates, Inc.
Attention: Kaye B. McDonald
201 Delaware Street
Greenville, SC 29605

Docket No. 01P-0130/CP2

Dear Ms. McDonald:

This is in response to your petition filed on April 25, 2001, requesting permission to file an Abbreviated New Drug Application (ANDA) for the following drug product: Hydrocodone Bitartrate and Acetaminophen Oral Solution, 10 mg/ 10 mL and 320 mg/ 10 mL. The listed drug product to which you refer in your petition is Hydrocodone Bitartrate and Acetaminophen Oral Solution, 7.5 mg/ 15 mL and 500 mg/ 15 mL, ANDA 40-182 held by Pharmaceutical Associates Inc.

This petition was reviewed pursuant to Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act (Act). Under Section 505(j)(2)(C)(i) of the Act such a petition will be approved unless the Food and Drug Administration (FDA) finds that investigations must be conducted to show the safety and effectiveness of the strength (concentration) of the proposed drug product which differs from the strength (concentration) of the listed drug product.

Your request involves a change in strength (concentration) and a change in the volume of drug product administered per dose (dosing regimen) from that of the listed drug product. The concentration of the listed drug is Hydrocodone Bitartrate, 7.5 mg /15 mL and Acetaminophen 500 mg /15 mL. The concentration of your proposed product expressed in its usual dosage (i.e., one tablespoonful or 15 mL) is Hydrocodone Bitartrate, 15 mg/ 15 mL and Acetaminophen, 480 mg/15 mL. The change in strength (concentration) that you request is the type of change that is authorized under Section 505(j)(2)(C) of the Act. However, the change in the volume of drug product administered per dose is not a change that is authorized under Section 505(j)(2)(C) of the Act. In addition, these changes raise safety issues.

The maximum single-dose of hydrocodone bitartrate is 10 mg. If a person was administered the usual dose for this drug product, 15 mL (i.e., one tablespoonful), the dose would exceed the maximum allowable single dose of Hydrocodone Bitartrate, 10 mg. If the dose that you propose, 10 mL (i.e., two teaspoonsful), was misread and a patient was administered two tablespoonsful (i.e., 30 ml) (a tablespoonful is the usual dose for this product), the dose that the patient would receive would be well above the maximum single-dose of hydrocodone bitartrate (i.e., 30 mg vs. 10 mg). If the maximum daily dose that you propose, 12 teaspoonsful, was misread as 12

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tablespoonsful, the patient would receive 180 mg of hydrocodone bitartrate (three times the maximum daily adult dose of 60 mg) and 5760 mg of acetaminophen, which exceeds the maximum daily adult dose of 4000 mg.

The FDA has determined that your proposed changes in strength and dosing regimen raise safety concerns, and the change you requested in dosing regimen is not petitionable. Therefore, FDA is denying the petition under Section 505(j)(2)(C)(i) because investigations are necessary to show the safety and effectiveness of the proposed drug product and because a change in dosing regimen is not authorized under Section 505(j)(2)(C) of the Act.

If you disagree with our determination concerning the acceptability of your petition as originally submitted, you may seek a reconsideration of the denial following the procedures set forth in 21 CFR 10.33. Requests for reconsideration must be based solely on the information contained in your original petition and must be submitted in accordance with 21 CFR Section 10.20, in the format outlined in Section 10.33 and no later than 30 days after the date of the decision involved. Petitions for reconsideration should be filed with the Dockets Management Branch at the address listed below. If there is additional information, not included as part of your original submission that you would like the FDA to consider, you should submit a new petition including all the necessary information to the Dockets Management Branch.

A copy of this letter denying your petition will be placed on public display in the Dockets Management Branch, Room 1061, Mail Stop HFA-305, 5630 Fishers Lane, Rockville, MD 20852.

Sincerely,



Gary J. Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research