





## DEPARTMENT OF HEALTH &amp; HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville MD 20857

Mikart, Inc.  
Attention: Carrie B. McDonald  
2090 Marietta Blvd., N.W.  
Atlanta, GA 30318

NOV 15 1994

Docket No. 93P-0346/CP1

Dear Madam:

This is in response to your petition filed on July 6, 1993, and your amendment dated October 8, 1993, requesting permission to file Abbreviated New Drug Applications (ANDAs) for the following drug products: Acetaminophen 325 mg, Butalbital 50 mg, Caffeine 40 mg and Hydrocodone Bitartrate 5 mg Capsules or Tablets. The listed drug product to which you refer in your petition is Fioricet<sup>®</sup> with Codeine Capsules (Acetaminophen 325 mg, Butalbital 50 mg, Caffeine 40 mg and Codeine 30 mg) manufactured by Sandoz Pharmaceuticals Corporation.

We have reviewed your petition under Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act (Act), and have determined that it is approved. This letter represents the Agency's determination that the above-referenced drug products are suitable for submission as ANDAs.

Regarding your proposed drug product in a tablet dosage form, your request involves a change in dosage form from that of the listed reference drug product (i.e., from a capsule to a tablet). In addition, you request a change in one active ingredient for another active ingredient of the same pharmacologic class in a fixed combination drug product (i.e., substituting an equipotent dose of hydrocodone bitartrate (HCB) for codeine phosphate). You also propose a drug product in a capsule dosage form. This request involves a change in one active ingredient for another active ingredient of the same pharmacologic class in a fixed combination drug product (i.e., substituting an equipotent dose of hydrocodone bitartrate (HCB) for codeine phosphate). The changes you request are the types of changes authorized under Section 505(j)(2)(C) of the Act.

Under Section 505(j)(2)(C)(i) of the Act, the Agency must approve a petition seeking a change in one active ingredient for another active ingredient of the same pharmacologic class in a fixed combination drug product, or a change in dosage form which differs from that of the listed reference drug product, unless it finds that investigations must be conducted to show the safety and effectiveness of the differing active ingredient or dosage form.

The Agency has determined that the changes you propose for these specific drug products do not pose questions of safety or effectiveness and concludes, therefore, that investigations are not necessary in this instance. The Agency has previously concluded that the potency ratio of codeine phosphate to hydrocodone bitartrate is 6:1. Based upon the 6:1 potency ratio, the proposed drug product HCB content (5 mg) is equivalent to the amount of codeine phosphate (30 mg) contained in the listed reference drug product. Because this dose of HCB is equivalent to the dose of codeine phosphate in the listed reference drug product and because the proposed drug products will have the same use, dose, and route of administration as the listed reference drug product, the single and total daily dose of HCB for these specific drug products will fall within the recommendations of an equivalent dose of codeine phosphate as cited in the approved drug product's labeling. In addition, if shown to meet the bioavailability requirements, the proposed drug products can be expected to have the same therapeutic effect as the listed reference drug product.

The approval of this petition to allow ANDAs to be submitted for the above-referenced drug products does not mean that the Agency has determined that ANDAs will be approved for the drug products. The determination that an ANDA will be approved is not made until the ANDA itself is submitted and reviewed by the Agency.

To permit review of your ANDA submissions, you must submit all information required under Sections 505(j)(2)(A) and (B) of the Act. To be approved, the drug products will, among other things, be required to meet current bioavailability requirements under Section 505(j)(2)(A)(iv) of the Act. We suggest that you contact the Acting Director, Division of Bioequivalence, at (301) 594-0345 to determine the specific requirements for these drug products. During the review of your applications, the Agency may require the submission of additional information.

The listed reference drug product to which you refer in your ANDAs must be the one upon which you based this petition. In addition, you should refer in your ANDAs to the appropriate petition docket number, cited above, and include a copy of this letter in the ANDA submissions.

A copy of this letter approving your petition will be placed on public display in the Dockets Management Branch, HFA-305, Room 1-23, Park Building, 12420 Parklawn Drive, Rockville, MD 20857.

Sincerely yours,



Douglas L. Sporn  
Acting Director  
Office of Generic Drugs  
Center for Drug Evaluation and Research.