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January 19, 2007

OVERNIGHT COURIER 1/19/07

Division of Dockets Management
Food and Drug Administration (HFA-305)
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

CITIZEN PETITION

Dear Sir or Madam:

The undersigned submits this petition, in quadruplicate, pursuant to Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act, and in accordance with 21 CFR 10.30 on behalf of a client requesting the Commissioner of the Food and Drug Administration to declare that the drug product, Acetaminophen, 400 mg, Butalbital, 50 mg, and Caffeine, 40 mg Capsules is suitable for consideration in an abbreviated new drug application (ANDA).

A. Action Requested

The petitioner requests that the Commissioner of the Food and Drug Administration declare that Acetaminophen, 400 mg, Butalbital, 50 mg, and Caffeine, 40 mg Capsules, is suitable for submission as an ANDA. The listed reference drug product (RLD), upon which this petition is based, is Esgic-Plus (Acetaminophen, Butalbital, and Caffeine Capsules 500 mg/50 mg/40mg, ANDA 40-085) currently held by Mikart as designated in the Orange Book. The petitioner also references Acetaminophen, Butalbital, and Caffeine Capsules 325 mg/50 mg/40 mg, ANDA 89-007 also held by Mikart in support of this petition. Therefore, the petitioner seeks only a change in strength of Acetaminophen component (from 500 mg to 400 mg) from that of the listed drug product.

B. Statement of Grounds

The Federal Food, Drug, and Cosmetic Act provides for the submission of an Abbreviated New Drug Application for a drug product that differs in dosage strength from that of the listed drug provided the FDA has approved a petition that proposed filing such an application.

The RLD, Esgic-Plus Capsules by Mikart is a capsule product containing 500 mg of Acetaminophen, 50 mg of Butalbital, and 40 mg of Caffeine. See copy of the page from the current Electronic Edition of the Approved Drug Products with Therapeutic Equivalence Evaluations (Attachment 1). The proposed drug product also represents a capsule dosage form, but containing 400 mg of Acetaminophen in combination with 50 mg of Butalbital and 40 mg of Caffeine. The petition is thus seeking a change in strength of only the Acetaminophen component (from 500 mg to 400 mg) from that of the RLD. Please note that the proposed change in strength represents a dosage strength that is consistent with the dosing recommendations of the RLD's approved labeling.

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The current dosing instructions in the approved labeling of the RLD are as follows:

“One capsule every 4 hours. Total daily dosage should not exceed 6 capsules.”

The RLD, therefore, has a total maximum Acetaminophen Exposure = 3 g/day well below the maximum 4 g permissible daily exposure level. The approved package insert labeling for Esgic-Plus Capsules (Acetaminophen, 500 mg, Butalbital, 50 mg and Caffeine, 40 mg capsules) is provided in Attachment 2.

The dosage for the proposed product (provided in Attachment 3) is “One capsule every 4 hours. Total daily dosage should not exceed 6 capsules.” The proposed product, therefore, has a total maximum acetaminophen exposure = 2.4 g/day also below the 4 g permissible daily exposure level. This dosage is consistent with the dosage approved in the reference listed drug product’s labeling and other FDA approved products and is consistent with safe and effective doses in the Tentative Final Monograph (TFM) for Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter Human Use.

In further support of approval of acetaminophen at a 400 mg dosage level, FDA has approved as safe and effective this dose in other combination products, such as Acetaminophen and Hydrocodone Bitartrate Tablets and Acetaminophen and Oxycodone Tablets. Please see Attachment 4.

In summary, the proposed change in strength of the non-narcotic component, Acetaminophen, from that of the reference-listed drug (i.e., change from 500 mg to 400 mg) will not raise questions of safety or efficacy of the proposed product. The indication remains unchanged and the proposed dosing is consistent with the dosing recommended in the approved labeling of the reference-listed drug product. Therefore, the Agency should conclude that clinical investigations are not necessary to demonstrate the proposed product’s safety or effectiveness.

There are no proposed changes in labeling with the exception of the obvious changes in strength sought in this petition. The uses, indications, warnings and directions for use will remain the same as that of the RLD. Draft labeling for the proposed product is included in Attachment 3, and the RLD’s approved labeling is provided in Attachment 2.

Therefore, the petitioner’s request for the Commissioner to find that a change in strength from 500 mg to 400 mg of Acetaminophen in the proposed Acetaminophen, Butalbital, and Caffeine Capsules, 400 mg/50 mg/40 mg should raise no questions of safety or effectiveness, and the Agency should approve the petition.

C. Environmental Impact

The petitioner claims a categorical exclusion under 21 CFR 25.31.

D. Economic Impact

The petitioner does not believe that this is applicable in this case, but will agree to provide such an analysis, if requested by the Agency.

E. Certification

The undersigned certifies that to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner, which are unfavorable to the petition.

Respectfully submitted,



Robert W. Pollock
Senior Vice President

- Attachments:
1. Approved Drug Products with Therapeutic Equivalence Evaluations, Electronic Orange Book listing, accessed 1/16/2007
 2. Approved labeling for reference listed drug, Esgic-Plus® Capsules
 3. Draft insert labeling for proposed Acetaminophen, Butalbital, and Caffeine Capsules 400 mg/50 mg/40 mg
 4. List of products approved in the Electronic Orange Book with 400 mg dosage strength of Acetaminophen, accessed 1/16/2007

cc: Craig Kiester (OGD)

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