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December 12, 2006

OVERNIGHT COURIER 12/12/06

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 Propoxyphene Hydrochloride, 65 mg and Acetaminophen, 325 mg Tablets 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 a Propoxyphene Hydrochloride 65 mg and Acetaminophen, 325 mg Tablet is suitable for submission as an ANDA. The listed reference drug product (RLD), upon which this petition is based, is Wygesic® (Propoxyphene Hydrochloride and Acetaminophen), 65 mg / 325 mg Tablets, ANDA 84-999, currently held by Leitner Pharmaceuticals as designated in the Orange Book. Therefore, the petitioner seeks a change in strength, of the Acetaminophen component (from 650 mg to 325 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, Wygesic® Tablets by Leitner Pharmaceuticals, is a tablet product containing 650 mg of acetaminophen and 65 mg of propoxyphene hydrochloride. See product listing for ANDA 84-899 from the electronic Orange Book also known as the *Approved Drug Products with Therapeutic Equivalence Evaluations*, accessed December 6, 2006, which lists the approval of the RLD (Attachment 1).

The proposed drug product represents a tablet dosage form containing 325 mg of acetaminophen in combination with 65 mg propoxyphene hydrochloride. The petition is thus seeking a change in strength of only the acetaminophen component (from 650 mg to 325 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:

> Wygesic® Tablets Dosage and Administration: "The usual dosage is 65 mg propoxyphene hydrochloride and 650 mg acetaminophen every 4 hours as needed for pain. The maximum recommended dose of propoxyphene hydrochloride is 390 mg per day."

Total maximum acetaminophen exposure from the approved RLD is 3.90 g / day (e.g., 6 x 650 mg / 65 mg), below the maximum 4 g permissible daily exposure level. The approved package insert for Wygesic® Tablets (propoxyphene hydrochloride, 65 mg and acetaminophen, 650 mg) is included in Attachment 2[1].

The dosage for the proposed product (see proposed package insert, Attachment 3) is: "One tablet every four hours as needed for pain. The maximum recommended dose of propoxyphene hydrochloride is 390 mg per day." Total maximum acetaminophen exposure of the proposed product is 1.95 g (6 x 325 mg / 65 mg product), again below the maximum 4 g daily exposure limit. This dosage is consistent with the dosage approved in the reference-listed drug product's labeling.

The proposed product will also provide the prescribing physician greater flexibility in dosing and pain management, especially in patients that must limit their intake of acetaminophen.

In further support of approval of acetaminophen at a 325 mg dosage level, the Agency has approved 325 mg as a safe and effective dose in other combination products, such as Acetaminophen and Hydrocodone Bitartrate Tablets and Acetaminophen and Oxycodone Hydrochloride Tablets. Please see Attachment 4.

In summary, the proposed change in strength of the non-narcotic component from that of the reference-listed drug (i.e., a change of acetaminophen from 650 mg to 325 mg) will not raise questions of the safety or efficacy of the proposed product. The indication remains unchanged and the proposed dosing is consistent with that recommended in the labeling of the approved 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.

Therefore, the petitioner's request for the Commissioner to find that a change in strength from 650 mg to 325 mg of Acetaminophen in the proposed Propoxyphene Hydrochloride and Acetaminophen Tablets, 65 mg / 325 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.

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[1] Please note that the labeling submitted was the only available labeling for Wygesic® that could be located. The new Leitner labeling was not available, however, the dosing information is not believed to have changed.

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 Pollock

Robert W. Pollock
Senior Vice President

RWP/pk

Attachments:

1. Approved Drug Products with Therapeutic Equivalence Evaluations, Electronic Orange Book listing accessed December 12, 2006
2. Labeling for reference-listed drug product (RLD), Wygesic® Tablets (Leitner)
3. Draft Insert Labeling Proposed for Propoxyphene Hydrochloride, 65 mg and Acetaminophen, 325 mg Tablets
4. List of products approved in Electronic Orange Book with 325 mg dosage strength of Acetaminophen

cc: Craig Kiester (OGD)

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