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CONSULTANTS TO THE PHARMACEUTICAL AND ALLIED INDUSTRIES

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February 28, 2007

OVERNIGHT COURIER 2/28/07

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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, Bisoprolol Fumarate and Hydrochlorothiazide Tablets, 5 mg / 12.5 mg, 10 mg / 12.5 mg, and 20 mg / 12.5 mg, 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 Bisoprolol Fumarate and Hydrochlorothiazide Tablets, 5 mg / 12.5 mg, 10 mg / 12.5 mg, and 20 mg / 12.5 mg, are suitable for submission as an ANDA. The reference-listed drug product (RLD), upon which this petition is based, is Ziac[®] (Bisoprolol Fumarate and Hydrochlorothiazide Tablets, NDA 20-186 held by Duramed Pharmaceuticals / Barr Laboratories, Inc., 10 mg / 6.25 mg. The petitioner also references the approval of Ziac[®] (Bisoprolol Fumarate and Hydrochlorothiazide Tablets) 2.5 mg / 6.25 mg and 5 mg / 6.25 mg, in support of this petition. Therefore, the petitioner seeks a change in strength (from 10 mg / 6.25 mg to include a 5 mg / 12.5 mg, 10 mg / 12.5 mg, and 20 mg / 12.5 mg strength) 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, Ziac[®] (Bisoprolol Fumarate and Hydrochlorothiazide Tablets), by Duramed Pharmaceuticals / Barr Laboratories, Inc., is a tablet product containing 10 mg of bisoprolol fumarate and 6.25 mg of hydrochlorothiazide (HCTZ). 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 tablet dosage form, but containing 5 mg / 12.5 mg, 10 mg / 12.5 mg, or 20 mg / 12.5 mg of bisoprolol fumarate and hydrochlorothiazide, respectively. The petition is thus seeking a change in strength (from 10 mg / 6.25 mg to include a 5 mg / 12.5 mg, 10 mg / 12.5 mg, and 20 mg / 12.5 mg strength) from that of the RLD.

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Please note that the proposed changes in strength represent dosage strengths that are contemplated in the approved labeling for the RLD. The currently approved labeling states:

"Antihypertensive therapy may be initiated with the lowest dose of ZIAC, one 2.5/6.25 mg tablet once daily. Subsequent titration (14 day intervals) may be carried out with ZIAC tablets up to the maximum recommended dose 20/12.5 mg (two 10/6.25 mg tablets) once daily, as appropriate."

The approved labeling clearly contemplates the use of the proposed higher strength, 20 mg / 12.5 mg of Bisoprolol / HCTZ albeit in a two-tablet dose (two 10 mg/6.25 mg tablets). Additionally, the approved labeling clearly indicates that the dose should be titrated as appropriate to provide the maximum benefit with minimal adverse effects. Because this drug product is not without the potential for significant adverse reactions, the proposed new strengths of the product would give the health care practitioner greater flexibility in selecting the most appropriate dose for the patient while minimizing potential adverse events. The availability of the additional strengths of Bisoprolol / HCTZ, 5 mg / 12.5 mg, 10 mg / 12.5 mg, and 20 mg / 12.5 mg, would provide greater flexibility to the healthcare practitioner in achieving the best tolerated dose for the patient while potentially improving compliance since the patient may need to take fewer tablets to achieve the appropriate prescribed dose.

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 products is included in Attachment 2, and the RLD's approved labeling is provided in Attachment 3.

Therefore, the petitioner's request for the Commissioner to find that a change in strength from 10 mg / 6.25 mg to 5 mg / 12.5 mg, 10 mg / 12.5 mg, and 20 mg / 12.5 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
Lachman Consultant Services, Inc.

RWP/pk

- Attachments:
1. Approved Drug Products with Therapeutic Equivalence Evaluations, accessed February 26, 2007
 2. Draft Labeling Proposed for Bisoprolol Fumarate and Hydrochlorothiazide Tablets, 5 mg / 12.5 mg, 10 mg / 12.5 mg, and 20 mg / 12.5 mg
 3. Labeling for the Reference-Listed Drug Ziac[®] (Bisoprolol Fumarate and Hydrochlorothiazide Tablets), by Duramed Pharmaceuticals / Barr Laboratories, Inc.

cc: Craig Kiester (OGD)

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