





DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

APR 29 2004 4 00 PM '04

The Weinberg Group, Inc.
Attention: Nicholas M. Fleischer, Ph.D.
1220 Nineteenth St. N.W., Suite 300
Washington, D.C. 20036-2400

Docket No. 02P-0414/CP1

Dear Dr. Fleischer:

This is in response to your petition filed on September 16, 2002, our letter dated February 3, 2004, and your amendment dated March 10, 2004. Your petition requests permission to file an Abbreviated New Drug Application (ANDA) for the following drug products: Cefuroxime Axetil Tablets for Oral Suspension, 125 mg and 250 mg. The listed drug products to which you refer in your petition are Ceftin® (Cefuroxime Axetil) Powder for Oral Suspension, 125 mg/5 mL and 250 mg/ 5 mL, NDA 50-672 held by GlaxoSmithKline.

This petition was reviewed pursuant to Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act (Act). Under Sections 505(j)(2)(C)(i) and (ii) 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 proposed drug product, or of any of its active ingredients, the route of administration, the dosage form, or strength which differ from the listed drug product; or that any drug product with a different active ingredient may not be adequately evaluated for approval as safe and effective on the basis of the information required to be submitted in an abbreviated application.

Your request involves a change in dosage form from that of the listed drug product (i.e., from powder for oral suspension to tablets for oral suspension). The change that you request is the type of change that is authorized under Section 505(j)(2)(C) of the Act.

The FDA has determined that your proposed change in dosage form raises questions of safety and effectiveness, and has concluded that clinical trials are required for this specific drug product. 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 products.

The listed drugs upon which you are basing your petition request are Ceftin Powder for Oral Suspension, 125 mg/5 mL and 250 mg/5 mL. These products are primarily utilized in pediatric patients ranging in age from 3 months to 12 years, according to the listed drug's label. Your

02P-0414

PDN1

02P-0414/CP1

Cefuroxime Axetil Tablets for Oral Suspension, 125 mg and 250 mg
The Weinberg Group Inc.

petition raises two different safety issues that require investigations. The first concerns dosage. The labeling for the listed drug provides that dosing for pediatric patients is calculated based upon the patient's weight (mg/kg) and the specific infection being treated. The labeling for the listed drug also provides specific amounts of water (in mLs) that are required to be administered for reconstitution of the product. By contrast, although your petition proposes dosing for pediatric patients calculated based upon the patients' weight (mg/kg) and the specific infection being treated, it does not provide for a specific amount of water to be administered for the dosage. Recommendations for administering your proposed product state that the tablet for oral suspension needs to be dissolved in one tablespoonful (15 mLs) to two ounces (60 mLs) of water. These figures range from less than half to greater than 50% more than the specific amount of water that the listed drug labeling recommends. Because your proposed product lacks a standard required numerical amount of diluent, unlike the listed drug, those administering the drug as directed will do so with varying concentrations of the product and without reference to the specific amount recommended for the listed drug. As a result, end concentrations of the product as presented for ingestion will vary among users and potentially even by the same user on different occasions. FDA has determined that for drugs dosed on a per weight (mg/kg) basis, the lack of a standardized end concentration poses safety concerns with regard to over/under dosing.

The second safety issue your petition raises is potential dosing errors that could produce inadvertent substitution of conventional Ceftin tablets and Ceftin tablets for oral suspension. The listed drug, a powder for oral suspension, is given to children, and Ceftin tablets 125 mg, 250 mg, and 500 mg are given to adults. Therefore, there is little likelihood of confusing the two dosage forms for the two populations. However, you propose to market a tablet for oral suspension for children. If your petition were granted, tablets would be available to administer Ceftin to both adults and children. As the product labels now note, Ceftin tablets and Ceftin Powder for Oral Suspension are not bioequivalent. Because tablets for oral suspension for pediatric use could be confused with bioinequivalent adult tablets, the proposed product has the potential for causing dosing errors in the adult population. Your proposed products purport to establish bioequivalence of Cefuroxime Axetil Tablets for Oral Suspension to the Powder for Oral Suspension formulations. However, adult dosages are based upon Ceftin Tablets, which have greater bioavailability than the Powder for Oral Suspension products. Were adults to receive your proposed product, they would potentially receive a subtherapeutic dose based upon the bioinequivalence of your proposed product in comparison to Ceftin Tablets.

We note that we have in the past approved petitions requesting changes in dosage form from a powder for oral suspension to tablets for oral suspension. Granting of such suitability petitions is warranted, if all other conditions are met, when the proposed changed dosage form can be determined to be safe and effective without the necessity of conducting investigations and when the proposed tablet for oral suspension is recommended to be administered based on the patient's weight and a specific amount of diluent. Where, as here, however, the tablet for oral suspension for one patient population could be administered in lieu of a bioinequivalent product designed for

02P-0414/CP1

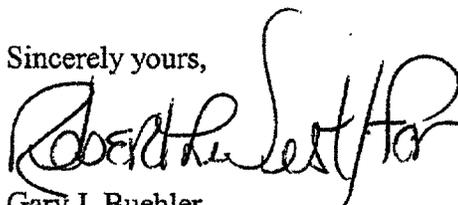
Cefuroxime Axetil Tablets for Oral Suspension, 125 mg and 250 mg
The Weinberg Group Inc.

a different population, the possibility of the administration of subtherapeutic doses precludes approval of the petition. Similarly, where, as here, the tablet for oral suspension, unlike the listed drug, is to be administered with varying amounts of diluent, the potential for under- or over-dosing raises safety concerns that were not present in certain previous petitions for a change in dosage form.

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 yours,



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