



THE WEINBERG GROUP INC.

OVERNIGHT COURIER

February 23, 2004

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

**Amendment to Citizen Petition
Docket Number 02P-0499/CP1
Inclusion of Pediatric Waiver Request**

Dear Sir or Madam:

The petition cited above was submitted on November 26, 2002. The petition requested the Commissioner of the Food and Drug Administration to declare that the drug product, Metformin Hydrochloride Tablets for Oral Solution, in strengths of 500 mg; 850 mg; and 1000 mg is suitable for submission in an abbreviated new drug application (ANDA). The petition was approved on May 14, 2003.

In December of 2003, Congress passed the Pediatric Research Equity Act of 2003 that amended the Federal Food, Drug and Cosmetic Act to provide the Agency authority to require drug firms to study certain drugs in pediatric patients, if the Agency felt that such study would provide beneficial health data for that patient population.

Reference is also made to the Agency's communication dated February 3, 2004, requiring submission of a waiver with supporting information and documentation in accordance with the provisions of Section 2 of PREA as an amendment to the suitability petition.

The Act provides a provision for a waiver from such requirement if:

(iii) the drug or biological product;

(I) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients; and

(II) is not likely to be used in a substantial number of pediatric patients.

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02P-0499

AMD 1

The petitioner hereby requests that a waiver from the conduct of pediatric studies be granted for this petition.

The reference listed drug, Glucophage® (metformin hydrochloride tablets, 1000 mg) is currently available in a conventional immediate-release tablet and is, according to the approved labeling, recommended for use as monotherapy as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes, including pediatric patients 10 years of age and older. The proposed product, Metformin Hydrochloride Tablets for Oral Solution is designed to provide a more convenient dosage form of metformin hydrochloride for patients who cannot swallow tablets. The petitioner believes that Metformin Hydrochloride Tablets for Oral Solution does not represent a meaningful therapeutic benefit over existing anti-diabetic therapies for the pediatric patient population.

The petitioner's product does not represent a meaningful therapeutic benefit over the Reference Listed Drug, Glucophage tablets, of Bristol Myers Squibb because the petitioner's product contains the same active ingredient and is labeled for the same indications as Glucophage tablets. As stated in the product labeling for Glucophage tablets, pediatric studies have been conducted. Therefore, the petitioner believes that additional clinical studies in the pediatric population with the petitioner's tablets for oral solution would not offer meaningful data demonstrating a therapeutic benefit over Glucophage tablets for the pediatric patient population for which it is indicated.

Furthermore, the petitioner has conducted a bioequivalence study comparing the petitioner's Metformin Hydrochloride Tablets for Oral Solution 1000 mg with Glucophage (1000 mg) tablets in the fasting and fed state in adult volunteers. The petitioner believes that the bioequivalence study conducted on adults should be adequate to demonstrate bioequivalence in children.

In addition, the following information supports the similarity of metformin pharmacokinetics between pediatric and adult patients. The sponsor of the anti-diabetic combination product, Glucovance® (metformin+glyburide), conducted a pediatric study which was a pharmacokinetic study to characterize single dose pharmacokinetics of metformin and glyburide in children and adolescents with type 2 diabetes following administration of Glucovance. This study concluded that the pharmacokinetics of metformin+glyburide were comparable between children and adolescent patients. In addition the sponsor made comparison of the pediatric pharmacokinetics with those in adults based on historic studies and concluded no significant difference in metformin and glyburide pharmacokinetics between the two groups. A copy of the Executive summary published in Summaries of Medical and Clinical Pharmacology Reviews of Pediatric Studies available from the FDA website is enclosed (Attachment A).

According to the approved labeling, the reference listed drug, Glucophage (metformin hydrochloride) tablets is recommended for use as monotherapy in pediatric patients 10 years of age and older. The petitioner's product, in line with Glucophage, is also indicated for use



in pediatric patients 10 years of age and older. Also, the petitioner believes that there will not be substantial use of Metformin Hydrochloride Tablets for Oral Solution in pediatric patients below 10 years of age. As per the information available from the Verispan PDDA database (Attachment B), approximately 24,000 pediatric patients between 0 and 9 years of age were reported to have visited a physician for diabetes during 2003, which indicates that the number of patients who would derive a meaningful therapeutic benefit from the indication for Metformin Hydrochloride Tablets for Oral Solution, as monotherapy as an adjunct to diet and exercise to improve glycemic control in patients with type 2 diabetes, is not substantial. Based on the limited pediatric patient population, the petitioner believes that there will not be substantial use of the product in pediatric patients below 10 years of age, and therefore does not warrant a pediatric study in the age group of 0-9 years.

For the reasons stated above and consistent with the provisions of the Pediatric Research Equity Act of 2003, the petitioner respectfully requests that this waiver be granted.

Very truly yours,



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NMF/kh

Enclosures

