LACHMAN CONSULTANT SERVICES, INC.
CONSULTANTS TO THE PHARMACEUTICAL AND ALLIED INDUSTRIES

1600 STEWART AVENUE, WESTBURY, NY 11590
(516) 222-6222 • FAX (516) 683-1887

August 26, 2003

OVERNIGHT COURIER 8/26/03

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

SUITABILITY PETITION

This petition is submitted pursuant to 21 CFR §10.20 and §10.30, as provided for in 21 CFR §314.93, and Section 505(j)(2)(C) of the Federal Food, Drug and Cosmetic Act to request the Commissioner of the Food and Drug Administration to declare that the drug product, Metformin Hydrochloride Extended-Release Tablets, 1000 mg is suitable for submission as an abbreviated new drug application (ANDA).

A. Action Requested

The petitioner requests that the Commissioner of the Food and Drug Administration declare that Metformin Hydrochloride Extended-Release (XR) Tablets, 1000 mg, is suitable for submission as an ANDA. The reference-listed drug product upon which this petition is based is Glucophage® XR (metformin hydrochloride) Extended-Release Tablets, 500 mg and 750mg, of Bristol-Myers Squibb Company (BMS) (NDA # 21-202), the listing of which can be found in the *Approved Drug Products with Therapeutic Equivalence Evaluations* 23rd Edition on page 3-238. The petitioner seeks a change in strength from that of the reference-listed drug (from 500 mg and 750 mg, to include a 1000 mg strength tablet). The active ingredient, the route of administration, doses and the recommendations for use are the same as those approved for that of the reference-listed drug product. The proposed product would, therefore, differ only in dosage strength from the approved marketed product.

The proposed drug product will be shown to be bioequivalent to the reference-listed drug product and that data will be submitted in the ANDA.

B. Statement of Grounds

The Federal Food, Drug and Cosmetic Act provides for the submission of an ANDA for a new drug that differs in dosage strength from that of a listed drug, provided the FDA has approved a petition that proposes the filing of such an application. This petition requests a change in strength for the proposed drug from that of the reference-listed drug.

The current package insert (revised April 2003) of **Glucophage® XR** states that there is no-fixed dosage regimen for the management of hyperglycemia in patients with Type 2 Diabetes with **Glucophage® or Glucophage® XR** or any other pharmacologic agent. Dosage of **Glucophage® or Glucophage® XR** must be individualized on the basis of both effectiveness and tolerance, while not exceeding the maximum recommended daily dose.

The recommended starting dose of Metformin Hydrochloride Extended-Release Tablets (Glucophage® XR) is 500 mg once daily with the evening meal. Dosage increases should be made in increments of 500 mg weekly up to a maximum of **2000 mg once daily** with the evening meal. It further states that if glycemic control is not achieved on Glucophage® XR 2000 mg once daily, a trial of **Glucophage® XR 1000 mg** given twice daily should be considered.

Therefore, a 1000 mg dose is clearly contemplated in the approved reference drug product's labeling. In addition, the availability of a 1000 mg extended-release tablet will decrease the number of dosage units a patient must take in order to achieve the recommended total daily dose of 2000 mg (two 1000 mg tablets vs. four 500 mg tablets), which may be preferable to certain patients.

The proposed petition thus seeks a change in strength (from a 500 mg and 750 mg extended-release tablets to include a 1000 mg extended-release tablet), where the administered dose will be the same as that recommended and approved for the reference-listed drug product.

The proposed 1000 mg extended-release tablet will offer the potential for a reduced number of dosage units to achieve the prescribed and desired dose that may prove to be more convenient and preferable to certain patients.

As discussed above, the proposed drug product will differ only in dosage strength. The indications, route of administration, intended patient population and recommendations for use shall remain the same as that of the approved reference-listed drug product, Glucophage® XR Tablets. Therefore, there can be no difference in the safety and efficacy of proposed Tablets.

The package insert for the approved reference-listed drug product, Glucophage® XR Tablets, manufactured by BMS, and the proposed package insert for the Metformin Hydrochloride Extended-Release Tablets, 1000 mg, are provided in Attachments 1 and 2, respectively.

C. Environmental Impact

An environmental assessment report on the action requested in this petition is not required under 21 CFR §25.31(a).

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 of its knowledge, 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 (dmi)

Robert W. Pollock, Vice President
Lachman Consultant Services, Inc.
1600 Stewart Avenue
Westbury, NY 11590

RWP/dmi

cc: M. Shimer

Attachment 1: Innovator Labeling
Attachment 2: Proposed Package Insert

R03P3238