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

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

June 18, 2003

OVERNIGHT COURIER 6/18/03

Dockets Management Branch
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 Glimepiride Tablets, 8 mg, is suitable for submission in an abbreviated new drug application (ANDA).

A. Action Requested

The petitioner requests that the Commissioner of the Food and Drug Administration make a determination that Glimepiride Tablets, 8 mg is suitable for submission as an ANDA. The listed reference drug product upon which this petition is based is Amaryl® (glimepiride) Tablets, 1 mg, 2 mg and 4 mg which appears in the 23rd edition of the *Approved Drug Products with Therapeutic Equivalence Evaluations* (more commonly known as the Orange Book) on page 3-176 (see Attachment I). Therefore, the petitioner seeks a change in strength (from 1 mg, 2 mg and 4 mg tablets to include an 8 mg tablet) 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 new drug that differs in strength from a listed drug provided the FDA has approved a petition that proposed the filing of such an application. This petition involves a change in strength for the proposed drug from that of the listed drug. The reference-listed drug (RLD) on which this petition is based is Amaryl® (glimepiride) Tablets manufactured by Aventis Pharmaceuticals. The proposed drug product differs only in strength from the reference-listed drug. The RLD is marketed as a tablet dosage form containing 1 mg, 2 mg or 4 mg of glimepiride. The proposed drug product represents the same dosage form and route of administration as the RLD.

2003P.0283 CP1

As mentioned above, Amaryl® (glimepiride) is currently approved for marketing as 1 mg, 2 mg and 4 mg tablets. The drug product is indicated "as an adjunct to diet and exercise to lower the blood glucose in patients with noninsulin-dependent (Type II) diabetes mellitus (NIDDM) whose hyperglycemia cannot be controlled by diet and exercise alone." As far as dosing and administration, the labeling stresses:

> "There is no fixed dosage regimen for the management of diabetes mellitus with Amaryl or any other hypoglycemic agent."

It is clear that each patient must be titrated to an effective dose of the drug product specific to the individual patient's needs and response to the medication. The proposed 8 mg drug product will offer an alternate higher dosage strength of Amaryl® (glimepiride) Tablets to treat those patients whose blood glucose cannot be controlled on a lower dose. The approved labeling for Amaryl® (glimepiride) Tablets states that:

> "[t]he usual starting dose of Amaryl as initial therapy is 1-2 mg once daily, administered with breakfast or the first main meal... The maximum starting dose is 2 mg."

However, since the drug must be titrated to a patient's response, the maintenance dose may be increased to 8 mg per day as is outlined in the labeling:

> "The usual maintenance dose is 1 – 4 mg once daily. The maximum recommended dose is **8 mg** once daily. After reaching a dose of 2 mg, dosage increases should be made in increments of no more than 2 mg at 1-2 week intervals based upon the patient's blood glucose response."

The approved labeling of the reference-listed drug product, therefore, clearly contemplates an 8 mg dose as patients may be titrated up to 8 mg of glimepiride to be taken in a single daily dose.

The availability of the proposed 8 mg tablet strength will provide the patient with a more convenient single tablet dosage and may be especially useful for patients who do not want to take multiple tablets to achieve a single dose. Availability of a single 8 mg tablet may also improve patient compliance, reduce the confusion often occurring when multiple tablets of the same product must be taken. In addition, since many NIDDM patients are taking other medications, reduction in the number of tablets a patient may need to take may also improve compliance and convenience for the patient. It will also provide the prescribing physician with a greater degree of flexibility in selecting the proper individualized maintenance dose for a specific patient's needs.

Therefore, the petitioner's request for the Commissioner to find that a change in strength for Amaryl® (glimepiride) Tablets, from 1 mg, 2 mg and 4 mg to include an 8 mg tablet, does not raise questions of safety or effectiveness and, therefore, the Agency should approve the petition.

A copy of the reference-listed drug labeling is included in Attachment 2. Draft labeling for the proposed drug product is included in Attachment 3. The proposed drug product represents the same uses, dosage, and indications as those for Amaryl® Tablets, the reference-listed drug.

C. Environmental Impact

An environmental assessment on the action requested in this petition qualifies for a categorical exclusion under 21 CFR 25.31.

D. Economic Impact

Pursuant to 21 CFR 10.30 (b), economic impact information is to be submitted only when requested by the Commissioner. We will gladly provide such information, if so requested.

E. Certification

The undersigned certifies that, to its best knowledge and belief, 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 PIC

Robert W. Pollock
Vice President

RWP/pk

Attachments: Attachment 1: Page 3-176, 23rd Edition of Orange Book
Attachment 2: Labeling of Reference-Listed Drug Amaryl®
Attachment 3: Draft Labeling for Glimepiride Tablets

cc: Martin Shimer (OGD)
Leon Lachman

P04P3169