DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-738/S-012
NDA 21-268/S-002

Biovail Laboratories, Inc.
c/o Biovail Technologies Limited
Attention: Ms. Beth Ferguson
3725 Concorde Parkway
Chantilly, VA 20151

Dear Ms. Ferguson:

Please refer to your supplemental new drug applications dated December 12, 2001 (NDA 20-738/S-012) and December 27, 2001 (NDA 21-268/S-002), submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Teveten (eprosartan mesylate), 400 and 600 mg Tablets (NDA 20-738) and Teveten HCT (eprosartan mesylate/hydrochlorothiazide), 600/12.5 and 600/25 mg Tablets (NDA 21-268).

We acknowledge receipt of your submissions dated October 28, 2002 and August 12, 2003. Your submissions of August 12, 2003 constituted a complete response to our October 18, 2002 approvable letter.

These "Changes Being Effected" supplemental new drug applications provide for final printed labeling revised as follows:

NDA 20-738/S-012 & NDA 21-268/S-002

1. Above the **DESCRIPTION** section, the phrase "**PRESCRIBING INFORMATION**" has been added.

2. The **CLINICAL PHARMACOLOGY**, **Special Populations, Renal Insufficiency** subsection has been revised to:

   Following administration of 600 mg once daily, there was a 70-90% increase in AUC, and a 30 to 50% increase in Cmax in moderate or severe renal impairment. The unbound eprosartan fractions increased by 35% and 59% in patients with moderate and severe renal impairment, respectively. No initial dosing adjustment is generally necessary in patients with moderate or severe renal impairment, with maximum dose not exceeding 600 mg daily. Eprosartan was poorly removed by hemodialysis (CL_{HD} <1 L/hr) (**See DOSAGE AND ADMINISTRATION**).

3. Under **CLINICAL PHARMACOLOGY**, **Pharmacokinetics, General** section, the 5th sentence has been changed to:

   The mean terminal elimination half-life of eprosartan following multiple oral doses of 600 mg was approximately 20 hours.

4. The **DOSAGE AND ADMINSTRATION, Elderly, Hepatically Impaired or Renally Impaired Patients** subsection has been revised to:

No initial dosing adjustment is generally necessary for elderly or hepatically impaired patients or those with renal impairment. No initial dosing adjustment is generally necessary in patients with moderate and severe renal impairment, with maximum dose not exceeding 600 mg daily.

NDA 20-738/S-012

1. Under **DESCRIPTION, Inactive Ingredients**, the word "hypromellose" has been substituted for the word "hydroxypropyl methylcellulose".

2. Under **ADVERSE REACTIONS**, the sentence "Rare cases of rhabdomyolysis have been reported in patients receiving angiotensin II receptor blockers" has been added.

3. Under **ADVERSE REACTIONS**, *Cardiovascular*, the event of "orthostatic hypotension" has been added so this subsection now reads as follows:

   Cardiovascular: angina pectoris, bradycardia, abnormal ECG, specific abnormal ECG, extrasystoles, atrial fibrillation, hypotension (including orthostatic hypotension), tachycardia, palpitations.

NDA 21-268/S-002

1. Under **ADVERSE REACTIONS**, **Eprosartan Mesylate**, *Cardiovascular*, the event of "orthostatic hypotension" has been added so this subsection now reads as follows:

   Cardiovascular: angina pectoris, bradycardia, abnormal ECG, specific abnormal ECG, extrasystoles, atrial fibrillation, hypotension (including orthostatic hypotension), tachycardia, palpitations.

We have completed the review of these supplemental applications and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted final printed labeling (package inserts included in your submissions of August 12, 2003). Accordingly, the supplemental applications are approved effective on the date of this letter.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact:

Mr. Edward Fromm
Regulatory Health Project Manager
(301) 594-5332

Sincerely,

{See appended electronic signature page}

Douglas C.Throckmorton M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Doug Throckmorton

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