DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022401/S-002

**SUPPLEMENT APPROVAL**

Boehringer Ingelheim Pharmaceuticals, Inc.
Attention: Ms. Terry Keyser
900 Ridgebury Road, PO Box 368
Ridgefield, CT 06877

Dear Ms. Keyser:

Please refer to your Supplemental New Drug Application (sNDA) dated December 11, 2009, received December 14, 2009, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Twynsta (telmisartan/amlodipine) 40/5, 40/10, 80/5, and 80/10 mg Tablets.

This Prior Approval supplemental new drug application provides for labeling revised as follows:

1. In the **HIGHLIGHTS OF PRESCRIBING INFORMATION** under **ADVERSE REACTIONS**, in the second sentence, the phrase "clinically meaningful orthostatic hypotension (6.3% vs 4.3%)," has been deleted.

2. In the Full Prescribing Information (FPI) under **6 ADVERSE REACTIONS**, **6.1 Clinical Trials Experience**, the following changes were made:

    a. Under the *TWYNSTA Tablets* subsection, the fourth paragraph has been changed from:

    The adverse reactions that occurred in the placebo-controlled factorial design trial in ≥2% of patients treated with TWYNSTA and at a higher incidence in TWYNSTA-treated patients (n=789) than placebo-treated patients (n=46) were peripheral edema (4.8% vs 0%), dizziness (3.0% vs 2.2%), clinically meaningful orthostatic hypotension (defined as a decrease in DBP >10 mmHg and/or decrease in SBP >20 mmHg) (6.3% vs 4.3%), and back pain (2.2% vs 0%). In addition, other adverse reactions that occurred in more than 1% of the patients treated with TWYNSTA tablets (n=789) were dizziness (2.0% vs 2.2% on placebo) and headache (1.4% vs 4.3% on placebo).

    To:

    The adverse reactions that occurred in the placebo-controlled factorial design trial in ≥2% of patients treated with TWYNSTA and at a higher incidence in TWYNSTA-treated patients (n=789) than placebo-treated patients (n=46) were peripheral edema (4.8% vs 0%), dizziness (3.0% vs 2.2%), and back pain (2.2% vs 0%). Edema (other than peripheral edema), hypotension, and syncope were reported in <2% of patients treated with TWYNSTA tablets.

b. Under the *Amlodipine* subsection, in the paragraph after Table 4, the following adverse events were added:

i. The term "change of bowel habit" has been added to the *Gastrointestinal* listings.

ii. The term "mood change" has been added to the *Psychiatric* listings.

3. Under **8.6 Hepatic Insufficiency** of the FPI, the number in parenthesis for the cross-references has been updated as follows:

a. In the first sentence, the number in parenthesis for the *Warnings and Precaution* cross-reference has been changed from 5.3 to 5.4 so that it now reads: "…[*see Dosage and Administration (2) and Warnings and Precautions (5.4)*]."

b. In the third sentence, the number in parenthesis for the *Dosage and Administration* cross-reference has been changed from 2.5 to 2.4 so that it now reads: "…[*see Dosage and Administration (2.4)*]."

4. The following minor editorial changes have been made:

a. The revision and copyright dates have been updated.

b. The internal label number has been updated.

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

**CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for the package insert, text for the patient package insert) and include the labeling changes proposed in any pending "Changes Being Effected" (CBE) supplements. Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including pending "Changes Being Effected" (CBE) supplements, for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format that includes the changes approved in this supplemental application.

At the time of your next printing, please italicize the brackets for all cross-references throughout the FPI , e.g., "[*see Dosage and Administration (2.5)*]" should be changed to "*[see Dosage and Administration (2.5)]*." This change should be reported in your next Annual Report.

**LETTERS TO HEALTH CARE PROFESSIONALS**

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA, to CDERMedWatchSafetyAlerts@fda.hhs.gov, and to the following address:

MedWatch Program
Office of Special Health Issues
Food and Drug Administration
10903 New Hampshire Ave
Building 32, Mail Stop 5353
Silver Spring, MD 20993

**REPORTING REQUIREMENTS**

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, please contact:

Quynh Nguyen, Pharm.D., RAC
Regulatory Health Project Manager
(301) 796-0510

Sincerely,

*{See appended electronic signature page}*

Norman Stockbridge, M.D., Ph.D.
Director
Division of Cardiovascular and Renal Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

| Application Type/Number | Submission Type/Number | Submitter Name | Product Name |
|---|---|---|---|
| NDA-22401 | SUPPL-2 | BOEHRINGER INGELHEIM PHARMACEUTICALS INC | TELMISARTAN/AMLODIPINE FIXED DOSE COM TB |

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

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/s/

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NORMAN L STOCKBRIDGE
07/27/2010