DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22-401 **NDA APPROVAL**

Boehringer Ingelheim Pharmaceuticals, Inc.
Attention: Ms. Monika Richter
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877

Dear Ms. Richter:

Please refer to your new drug application (NDA) dated December 18, 2008, received December 18, 2008, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Twynsta (telmisartan/amlodipine) 40/5, 40/10, 80/5, 80/10 mg Tablets.

We acknowledge receipt of your submissions dated February 5, 6, and 17, March 4, April 16 and 17, July 7, 10 (two), 15, and 24, August 14, September 8, 25 (two), and October 6 (two), 2009.

This new drug application provides for the use of Tywnsta Tablets for the treatment of hypertension, alone or with other antihypertensive agents. Twynsta Tablets may also be used as initial therapy in patients who are likely to need multiple drugs to achieve their blood pressure goals.

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

We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit 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 and text for the patient package insert). For administrative purposes, please designate this submission, "**SPL for approved NDA 22-401**."

CARTON AND IMMEDIATE CONTAINER LABELS

We acknowledge your July 10 and October 6, 2009 submissions containing final printed carton and container labels submitted electronically. At the time of your next printing, please revise the outer cartons for all strengths to add a statement with the amount of amlodipine besylate present and add an asterisk next to the strength and statement. This change may be reported in your next annual report.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are

required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for this application because this product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients **and** is not likely to be used in a substantial number of pediatric patients.

Twynsta is a combination antihypertensive agent. There are single agent products studied and labeled for use in pediatrics, and most pediatric patients are not treated with combination antihypertensives (supported by **The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents**, *Pediatrics* 2004;114;555-576).

QUALITY

As agreed upon during the teleconference on October 2, 2009, you will adopt the following dissolution methodology/specification for amlodipine:

Medium: 500 mL 0.01 N HCl, pH 2
Apparatus: paddle with 75 rpm
Specification: Q of (b) (4) at 30 minutes

POSTMARKETING COMMITMENTS

We remind you of your postmarketing commitments in your submission dated October 6, 2009. These commitments are listed below.

1. As discussed and agreed with the Division of Pre-Marketing Assessment I, Office of New Drug Quality Assessment in the teleconference held on October 2, 2009, the dissolution specification for telmisartan will remain at Q=(b) (4) at 30 minutes. Within one year of NDA approval, Boehringer Ingelheim Pharmaceuticals, Inc. (BIPI) commits to change the dissolution specification for telmisartan to Q=(b) (4) at 20 minutes unless BIPI submits data within this time period to show that the change is not supported.

2. As discussed and agreed with the Division of Pre-Marketing Assessment I, Office of New Drug Quality Assessment in the teleconference held on October 2, 2009, for amlodipine, BIPI commits to generate the necessary data post-approval to determine if the phosphate buffer pH 6.8 method is appropriate for the product. BIPI will collect stability data on the primary stability batches at 36 months as well as the ongoing stability for the first three production batches at 18 months per the post approval stability commitment, using both the dissolution media 0.01 N HCl at pH 2 and phosphate buffer at pH 6.8. Within one year post approval, BIPI will provide FDA with the data and an assessment as to whether the testing conditions using phosphate buffer pH 6.8 are appropriate for determination of amlodipine dissolution in telmisartan/amlodipine tablets. Should the dissolution method using the phosphate buffer at pH 6.8 be deemed suitable, an appropriate specification will be presented along with justification for the acceptance criteria.

Submit chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, and any changes in plans since the last annual report. All submissions, including supplements, relating to these postmarketing study commitments

should be prominently labeled "**Postmarketing Study Commitment Protocol**," "**Postmarketing Study Commitment Final Report**," or "**Postmarketing Study Commitment Correspondence**."

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

Please submit one market package of the drug product when it is available.

LETTERS TO HEALTH CARE PROFESSIONALS

If you 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 an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
Suite 12B-05
5600 Fishers Lane
Rockville, MD 20857

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: Agreed-upon labeling text