

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-314

APPROVAL LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration
Rockville, MD 20857

NDA 22-314

NDA APPROVAL

Novartis Pharmaceuticals Corporation
Attention: Ms. Nancy A. Price
One Health Plaza
East Hanover, New Jersey 07936-1080

Dear Ms. Price:

Please refer to your new drug application (NDA) dated June 30, 2008 submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Exforge HCT (amlodipine, valsartan, hydrochlorothiazide) 5/160/12.5, 10/160/12.5, 5/160/25, 10/160/25 and 10/320/25 mg Tablets.

We acknowledge receipt of your submissions dated August 12, 25 (two), September 18, October 7, 15, 21, 30, November 21, December 22, 2008 and March 3, 6, 26, 30, April 13, 17 (two), 20, and 24, 2009.

This new drug application provides for the use of Exforge HCT Tablets for the treatment of hypertension.

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 (package insert and patient package insert) and in your April 13 and 17, 2009 submissions containing final electronic carton and container labels.

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.

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/oc/datacouncil/spl.html> that is identical to the enclosed labeling (text for the package insert and the patient package insert). Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "SPL for approved NDA 22-314."

A 24-month expiration period is granted for all strengths of the drug product packaged in 30 count (90 cc), 90 count and 100 count (175 cc) — bottles. A 12-month expiration period is granted for all strengths of the drug product packaged in blisters.

b(4)

b(4)

The carton and bottle labels for the Exforge HCT tablets in 100 count — bottles should be submitted as a labeling supplement before marketing them.

b(4)

We acknowledge your commitment to update and submit the final agreed-upon drug product specification documents in the first annual report. Include "non-scored" in the drug product description in the specification to be consistent with drug product description in sections 3 and 16 of the package insert.

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.

Exforge HCT 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).

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(s) 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(s), 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 www.fda.gov/cder/ddmac.

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 12B05
5600 Fishers Lane
Rockville, MD 20857

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

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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 PI and PPI

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

/s/

Ellis Unger
4/30/2009 09:28:15 AM
for Norman Stockbridge, M.D., Ph.D.