**CENTER FOR DRUG EVALUATION AND RESEARCH**

**Approval Package for:**

***APPLICATION NUMBER:***

# 202331Orig1s000

***Trade Name:*** Edarbyclor Tablets, 40/12.5 and 40/25 mg

***Generic Name:*** azilsartan medoxomil and chlorthalidone

***Sponsor:*** Takeda Pharmaceuticals North America

***Approval Date:*** December 20, 2011

***Indications:*** treatment of hypertension, to lower blood pressure. Edarbyclor may be used in patients whose blood pressure is not adequately controlled on monotherapy. Edarbyclor may be used as initial therapy if a patient is likely to need multiple drugs to achieve blood pressure goals.

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# 202331Orig1s000

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***APPLICATION NUMBER:***

# 202331Orig1s000

# APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202331

**NDA APPROVAL**

Takeda Pharmaceuticals North America
Attention: Ms. Beth-Anne Knapp, MBA, RAC
One Takeda Parkway
Deerfield, IL 60015

Dear Ms. Knapp:

Please refer to your New Drug Application (NDA) dated February 24, 2011, received February 24, 2011, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Edarbyclor (azilsartan medoxomil and chlorthalidone) Tablets, 40/12.5 and 40/25 mg.

We acknowledge receipt of your amendments dated March 3 and 9, April 1, 6, 7, 8, 13, 19 and 22, May 3, 4, 23, 26 and 31, June 1, 17 and 23, July 1, 13 and 28, Aug 19 and 30, October 7, 18, 24, (two) and 27, November 4, 14, 21 and 29, and December 8, 13 and 16, 2011.

This new drug application provides for the use of Edarbyclor (azilsartan medoxomil and chlorthalidone) Tablets for the treatment of hypertension, to lower blood pressure. Edarbyclor may be used in patients whose blood pressure is not adequately controlled on monotherapy. Edarbyclor may be used as initial therapy if a patient is likely to need multiple drugs to achieve 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.

## CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert, text for the patient package insert). 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/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

## CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels submitted on November 29, 2011, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry

titled "Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)." Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 202-331**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

**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. Edarbyclor 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).

**POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B**

We remind you of your postmarketing commitment:

1854-1 Provide a supplement including the *in vitro* dissolution data gathered for all strengths of azilsartan medoxomil and chlorthalidone from the batches manufactured during the first year following approval date. If the dissolution Stage 2 testing is observed to be (b) (4) provide a justification to support the re-evaluation of the dissolution acceptance criteria for all strengths of both azilsartan medoxomil and chlorthalidone.

The timetable you submitted on October 18, 2011 and your email dated November 7, 2011, states that you will conduct this study according to the following schedule:

Final Report Submission: December 24, 2012

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, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing 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.

## 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

ENCLOSURES:
Content of Labeling
Carton and Container Labeling

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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
12/20/2011