DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 019888/S-067

SUPPLEMENT APPROVAL

Alvogen Malta Operations Ltd.
c/o Alvogen Pine Brook LLC
Attention: Patricia Jaworski, US Agent
Vice President, Regulatory Affairs
10 Bloomfield Avenue, Building B
Pine Brook, NJ 07058

Dear Ms. Jaworski:

Please refer to your Supplemental New Drug Application (sNDA) dated and received June 7, 2017, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Zestoretic (lisinopril/hydrochlorothiazide) 10/12.5 mg, 20/12.5 mg, 20/25 mg Tablets.

This Prior Approval supplemental new drug application provides for the following revisions to the approved labeling:

1. Under **CONTRAINDICATIONS**, the following text was added:

   ZESTORETIC is contraindicated in combination with a neprilysin inhibitor (e.g., sacubitril). Do not administer ZESTORETIC within 36 hours of switching to or from sacubitril/valsartan, a neprilysin inhibitor (see WARNINGS).

2. Under **WARNINGS**, Lisinopril, the following text was added to the third paragraph:

   Patients receiving coadministration of ACE inhibitor and mTOR (mammalian target of rapamycin) inhibitor (e.g., temsirolimus, sirolimus, everolimus) therapy or a neprilysin inhibitor may be at increased risk for angioedema (see PRECAUTIONS).

3. Under **PRECAUTIONS, Drug Interactions**, the following section was added:

   Neprilysin Inhibitors
   Patients taking concomitant neprilysin inhibitors may be at increased risk for angioedema. (see WARNINGS)

4. Several formatting and other editorial changes were noted throughout the label.

5. The revision date and version number were updated.

There are no other changes from the last approved package insert and patient package insert.

APPROVAL & LABELING

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

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to:

OPDP Regulatory Project Manager
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion (OPDP)
5901-B Ammendale Road
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf. Information and Instructions for completing the form can be found at http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above, by fax to 301-847-8444, or electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft guidance for industry (available at:

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf).

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 call:

Lori Anne Wachter, RN, BSN, RAC
Regulatory Project Manager for Safety
(301) 796-3975

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, PharmD.
Deputy Director for Safety
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling

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

/s/

MARY R SOUTHWORTH
07/21/2017