



NDA 19-888/S-040

AstraZeneca Pharmaceuticals LP
Attention: Ms. Judy W. Firor
1800 Concord Pike
PO Box 8355
Wilmington, DE 19803-8355

Dear Ms. Judy Firor:

Please refer to your supplemental new drug application dated February 14, 2005, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zestoretic (lisinopril/hctz) 20/12.5, 20/25, and 10/12.5 mg Tablets.

This "Changes Being Effected" supplemental new drug application provides for revisions to the **WARNINGS/Head and Neck Angioedema** and **WARNINGS/Hepatic Failure** subsections based on post-marketing information.

This supplemental new drug application provides for electronic final printed labeling with the following revisions:

1. Under the **WARNINGS/Head and Neck Angioedema** subsection

From:

In instances where swelling has been confined to the face and lips the condition has generally resolved without treatment, although antihistamines have been useful in relieving symptoms. Angioedema associated with laryngeal edema may be fatal.

To:

Even in those instances where swelling of only the tongue is involved, without respiratory distress, patients may require prolonged observation since treatment with antihistamines and corticosteroids may not be sufficient. Very rarely, fatalities have been reported due to angioedema associated with laryngeal edema or tongue edema. Patients with involvement of the tongue, glottis or larynx are likely to experience airway obstruction, especially those with a history of airway surgery.

2. Under the **WARNINGS/Hepatic Failure** subsection the phrase "or hepatitis" has been added to the following sentence:

Rarely, ACE inhibitors have been associated with a syndrome that starts with cholestatic jaundice or hepatitis and progresses to fulminant hepatic necrosis and (sometimes) death.

We have completed our review of this application, and it is approved, effective on the date of this letter, for use as recommended in the electronic final printed labeling (FPL) submitted on February 14, 2005.

We also note the following minor editorial revisions under the **HOW SUPPLIED** section of the labeling:

*AN69 is a registered trademark of Hospital Ltd.

Zestoretic is a trademark of the AstraZeneca group of companies.

If you issue a letter communicating important information about this drug product (i.e., a “Dear Health Care Professional” letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
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:

Alisea Sermon, Pharm.D.
Regulatory Project Manager
(301) 594-5334

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D.
Acting Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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

/s/

Norman Stockbridge
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