DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 18-760/S-024

AstraZeneca Pharmaceuticals LP
Attention: Ms. Cindy M. Lancaster
1800 Concord Pike
PO Box 8355
Wilmington, DE 19803-8355

Dear Ms. Lancaster:

Please refer to your supplemental new drug application dated August 23, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Tenoretic (atenolol and chlorthalidone) 50/25 and 100/25 mg Tablets.

We acknowledge receipt of your submission dated June 4, 2002. Your submission of June 4, 2002 constituted a complete response to our February 22, 2002 action letter.

This supplemental new drug application provides for final printed labeling (FPL) revised as follows:

1. The addition of the following paragraphs to the CLINICAL PHARMACOLOGY section:

   Atenolol Geriatric Pharmacology: In general, elderly patients present higher atenolol plasma levels with total clearance values about 50% lower than younger subjects. The half-life is markedly longer in the elderly compared to younger subjects. The reduction in atenolol clearance follows the general trend that elimination of renally excreted drugs is decreased with increasing age.

   Chlorthalidone geriatric pharmacology: In a study conducted in four elderly (73-93 years) hypertensive male and female patients receiving on day one, 25mg chlorthalidone in the morning and from day 11 to 69 (8 weeks), 25 mg chlorthalidone every second day, the peak concentration was more than three times higher on average at the end of the treatment than at the beginning (19.90 ± 3.28 v. 5.95 ± 1.3µmol/l). The apparent elimination half-life of chlorthalidone was more than doubled in elderly subjects as compared to young healthy volunteers: 110 vs. 50 hours. The limited data from this study suggest that the elimination of chlorthalidone is decreased in elderly patients due to age or hypertensive disease.

We completed our review of this supplemental new drug application. It is approved, effective on the date of this letter, for use as recommended in the final printed labeling submitted on June 4, 2002.

At the time of the next printing, please make the following change:

1. Delete the following paragraph in the CLINICAL PHARMACOLOGY section:

   Chlorthalidone geriatric pharmacology: In a study conducted in four elderly (73-93 years) hypertensive male and female patients receiving on day one, 25mg chlorthalidone in the morning and from day 11 to 69 (8 weeks), 25 mg chlorthalidone every second day, the peak concentration was more than three times higher on average at the end of the treatment than at the beginning (19.90 ± 3.28 v. 5.95 ± 1.3µmol/l). The apparent elimination half-life of chlorthalidone was more than doubled in elderly subjects as compared to young healthy volunteers: 110 vs. 50 hours. The limited data from this study suggest that the elimination of chlorthalidone is decreased in elderly patients due to age or hypertensive disease.

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, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please call:

Ms. Melissa Robb
Regulatory Project Manager
(301) 594-5313

Sincerely,

{See appended electronic signature page}

Douglas C. Throckmorton, M.D.
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/

Doug Throckmorton

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