DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 19-058/S-015

AstraZeneca Pharmaceuticals LP
Attention: Ms. Cindy M. Lancaster
1800 Concord Pike
P.O. 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 Tenormin (atenolol) 5 mg Injection.

We acknowledge receipt of your submissions dated March 8, 2002, June 4, 2002 and November 27, 2002. Your submission of November 27, 2002 constituted a complete response to our February 22, 2002 action letter.

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

1. The addition of a Geriatric Use subsection to the PRECAUTIONS section of the labeling as follows:

   Geriatric Use

   Hypertension and Angina Pectoris Due to Coronary Atherosclerosis:
   Clinical studies of TENORMIN did not include sufficient number of patients aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

   Acute Myocardial Infarction
   Of the 8,037 patients with suspected acute myocardial infarction randomized to TENORMIN in the ISIS-1 trial (See CLINICAL PHARMACOLOGY), 33% (2,644) were 65 years of age and older. It was not possible to identify significant differences in efficacy and safety between older and younger patients; however, elderly patients with systolic blood pressure <120 mmHg seemed less likely to benefit (See INDICATIONS AND USAGE).

   In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy. Evaluation of patients with hypertension or myocardial infarction should always include assessment of renal function.

2. The addition of the following paragraph to the CLINICAL PHARMACOLGY section of the labeling:

   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 the elimination of renally excreted drugs is decreased with increasing age.

3. Under the DOSAGE AND ADMINISTRATION/Elderly Patients or Patients with Renal Impairment, the second sentence of the first paragraph has been changed from:

   Some reduction in dosage may also be appropriate for the elderly, since decreased kidney function is a physiologic consequence of aging.

   to:

   In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting greater frequency of decreased hepatic, renal or cardiac function, and of concomitant disease or other drug therapy. Evaluation of patients with hypertension or myocardial infarction should always include assessment of renal function.

4. The addition of the following sentence to the ADVERSE REACTIONS section:

   Most adverse effects have been mild and transient.

5. In the DOSAGE AND ADMINISTRATION section, Elderly Patients or Patients with Renal Impairment subsection, the following sentence has been added at the end of the second paragraph:

   Atenolol excretion would be expected to decrease with advancing age.

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 November 27, 2002.

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 Health 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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