



NDA 20-668/S-012

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

Dear Ms. Firor:

Please refer to your supplemental new drug application dated June 30, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for LEXXEL (enalapril maleate-felodipine ER) 5-2.5 and 5-5 mg Tablets.

We also acknowledge receipt of your electronic labeling submission dated December 14 and 21, 2004.

This supplement provides for revisions to delete the text related to the 5-2.5 mg tablet in the **DESCRIPTION, DOSAGE AND ADMINISTRATION**, and **HOW SUPPLIED** sections of the labeling, as AstraZeneca is proposing to (b) (4) ----- of LEXXEL.

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 labeling text submitted on December 21, 2004 and with the revisions listed below.

1. Under **PRECAUTIONS/Geriatric Use**, add “Elderly patients may have elevated plasma concentrations of felodipine and may respond to lower doses of felodipine” as the third sentence. The subsection should read as follows:

Clinical studies of LEXXEL did not include sufficient numbers of subjects 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. Elderly patients may have elevated plasma concentrations of felodipine and may respond to lower doses of felodipine. 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 (see **CLINICAL PHARMACOLOGY** and **DOSAGE AND ADMINISTRATION** for information on the individual components of LEXXEL).

This drug is known to be substantially excreted by the kidney and the risk of toxic reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection.

Evaluation of the hypertensive patient should always include assessment of renal function (see **CLINICAL PHARMACOLOGY**).

The final printed labeling (FPL) must be identical, and include the revision indicated, to the text for the package insert dated December 21, 2004. These revisions are terms of the approval of this application.

Please submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDA. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 20-668/S-012." Approval of this submission by FDA is not required before the labeling is used.

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 Ms. Denise M. Hinton, Regulatory Health Project Manager, at (301) 594-5333.

Sincerely,

*{See appended electronic signature page}*

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

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