



NDA 20-668/S-011

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

Dear Ms. Firor:

Please refer to your supplemental new drug application dated December 11, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for LEXXEL (enalapril maleate/felodipine ER) 5/2.5 and 5/5mg Tablets.

This "Changes Being Effected" supplemental new drug application provides for electronic Final Printed Labeling with revisions to the **PRECAUTIONS/Drug Interactions** section of the labeling. Information has been added to include information regarding a tacrolimus drug interaction and revisions noted in the approval letter, dated June 11, 2003. It also includes updates to the NDC and revision date.

The proposed changes to the labeling are as follows:

1. Under **PRECAUTIONS/Drug Interactions**, enalapril maleate was added in parenthesis after VASOTEC in the second paragraph of the *Non-steroidal Anti-inflammatory Agents* subsection. The paragraph was revised to read as follows:

In a clinical pharmacology study, indomethacin or sulindac was administered to hypertensive patients receiving VASOTEC (enalapril maleate). In this study there was no evidence of a blunting of the antihypertensive action of VASOTEC (enalapril maleate). However, reports suggest that NSAIDS may diminish the antihypertensive effect of ACE-inhibitors. This interaction should be given consideration in patients taking NSAIDS concomitantly with ACE-inhibitors.

2. Under **PRECAUTIONS/Drug Interactions**, the following was added after the *Anticonvulsants* paragraph:

Tacrolimus- Felodipine may increase the blood concentration of tacrolimus. When given concomitantly with felodipine, the tacrolimus blood concentration should be followed and the tacrolimus dose may need to be adjusted.

3. Updates to the package insert are as follows:
 - a. The trademark date, 2003, was added after ©AstraZeneca 2002.
 - b. The Package Insert revision date was changed from 08/02 to 11/03.

- c. The NDC was changed from 9176507 to 9176508 and 620008-07 was changed to 620008-08.

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 submitted final printed labeling (package insert included in your electronic submission dated December 11, 2003).

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
(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

ENCLOSURE

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/s/

Norman Stockbridge
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