CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 19777/S30

CORRESPONDENCE

ZENECA
Pharmaceuticals
A Business Unit of Zeneca Inc.

1800 Concord Pike
PO Box 15437
Wilmington, DE 19850-5437

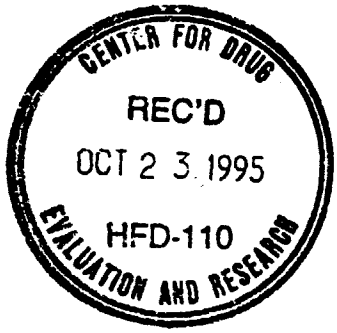
NDA NO. 19-777 REF. NO. S-030

NDA SUPPL FOR SLR

SENT VIA AIRBORNE EXPRESS

OCT 20 1995

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Cardio-Renal Drug Products
Attention: Document Control Room, HFD-110
1451 Rockville Pike
Rockville, MD 20852



Dear Sir/Madam:

Re: ZESTRIL® (lisinopril) Tablets
NDA 19-777
Special Supplement - Changes Being Effected

Pursuant to 21 CFR 314.70(c)(2)(i), we take this opportunity to provide the Agency with final printed labeling for ZESTRIL® (lisinopril) Tablets as Rev F 09/95 (Tab 1). This labeling will be implemented into production activities beginning the week of October 30, 1995.

For your convenience, enclosed as Tab 2 is a 3-column review document which clearly illustrates the changes being made in this supplement. The left column represents approved labeling; the middle column represents the present labeling changes; and the right column provides supporting comments, when applicable.

The specific labeling changes are:

ADVERSE REACTIONS - Skin

In response to an FDA letter dated May 30, 1995 and after review of the Zeneca safety database, this subsection has been revised as indicated by the underscored language following below:

"Urticaria, alopecia, herpes zoster, photosensitivity, lesions, skin infections, pemphigus, erythema, flushing, diaphoresis. Other severe skin reactions have been reported rarely, including toxic epidermal necrolysis and Stevens-Johnson syndrome; causal relationship has not been established."

Please refer to page 25 of the enclosed 3-column review document. Justification for language pertaining to toxic epidermal necrolysis and Stevens-Johnson Syndrome is enclosed as Tab 3.

ORIGINAL

DESCRIPTION

The third paragraph has been revised to include mention of the availability of ZESTRIL Tablets 2.5 mg, which will now be distributed for the first time in November 1995.

Added as the fifth paragraph in this section under "Inactive Ingredients" is the following:

"2.5 mg tablets - calcium phosphate, magnesium stearate, mannitol, starch."

See pages 1 and 2 of the enclosed 3-column review document. These labeling revisions pertaining to ZESTRIL Tablets 2.5 mg were previously approved as S-016 on April 29, 1993.

HOW SUPPLIED

The following has been added as the first paragraph of this section:

"**2.5 mg Tablets (NDC 0310-0135)** white, oval, biconvex, uncoated tablets identified as "ZESTRIL 2 1/2" on one side and "135" on the other side are supplied in bottles of 100 tablets. ZESTRIL 2.5 mg Tablets are manufactured by Zeneca Pharmaceuticals."

See page 31 of the enclosed 3-column review document. This labeling revision pertaining to ZESTRIL Tablets 2.5 mg was previously approved as S-016 on April 29, 1993.

Please contact me if you need additional information.

Sincerely,

Timothy K. Ressler
Assistant Manager, Marketed Products
Drug Regulatory Affairs Department
(302) 886-2123
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TKR/RJO/jr/3652/84
Enclosure