

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPROVAL PACKAGE FOR:**

**APPLICATION NUMBER**

**19-777/S-044**

**Approval Letter(s)**



NDA 19-777/S-042 & 044

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

Dear Ms. Firor:

Please refer to your supplemental new drug applications dated July 17, 2000 (S-042) and November 2, 2001 (S-044) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zestril (lisinopril) 2.5, 5, 10, 20, 30 and 40 mg Tablets.

We acknowledge receipt of your submissions dated January 23 (S-042) and August 6, 2002 (S-044).

Your submission dated June 12, 2003 constituted a complete response to our July 25, 2002 action letter.

These supplemental new drug applications propose changes in the **CLINICAL PHARMACOLOGY, INDICATIONS AND USAGE, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, ADVERSE REACTIONS, OVERDOSAGE** and **DOSAGE AND ADMINISTRATION** sections of the labeling concerning the use of Zestril (lisinopril) in pediatric patients and revised safety information.

We have completed our review of this supplemental new drug application, and it is approved, effective on the date of this letter, for use as recommended in the final printed labeling (FPL) submitted on June 13, 2003.

We also note revisions in the labeling in response to our approval letters dated October 17, 2002 and January 22, 2003 that provided for changes to the **WARNINGS/Head and Neck Angioedema** and **Intestinal Angioedema** subsections.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

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 contact:

Alisea Sermon, Pharm.D.  
Regulatory Project Manager  
(301) 594-5334

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

Enclosure

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/s/

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Doug Throckmorton  
7/1/03 11:30:51 AM

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPROVAL PACKAGE FOR:**

**APPLICATION NUMBER**

**19-777/S-044**

**Approvable Letter (S)**



NDA 19-777/S-042  
/S-044

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 July 17, 2000 (S-042) and November 2, 2001 (S-044) supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Zestril (lisinopril) Tablet, 2.5, 5, 10, 20, 30 and 40 mg.

We acknowledge receipt of your submission dated January 23, 2002.

Supplemental new drug application S-042 proposes changes to include revised safety information under the **CONTRAINDICATIONS, PRECAUTIONS, and OVERDOSAGE** sections of the labeling.

Supplemental new drug application S-044 proposes changes in the **CLINICAL PHARMACOLOGY, PRECAUTIONS, ADVERSE REACTIONS, and DOSAGE AND ADMINISTRATION** sections of the labeling concerning the use of Zestril in pediatric patients.

We have completed the review of these applications, as amended, and they are approvable. Before these applications may be approved, however, it will be necessary for you to submit final printed labeling (FPL) for the drug. The labeling should be identical in content to the enclosed labeling (text for the package insert).

In addition, all previous revisions as reflected in the most recently approved labeling must be included. To facilitate review of your submission, please provide a highlighted or marked-up copy that shows the changes that are being made.

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). Alternatively, you may submit 20 paper copies of the FPL, ten of which individually mounted on heavy weight paper or similar material.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

This product may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed with these changes prior to approval of this supplemental application.

If you have any questions, please contact:

Quynh Nguyen, Pharm.D.  
Regulatory Health Project Manager  
(301) 594-5311

Sincerely

/S/

*{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

Enclosure

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/s/

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Doug Throckmorton  
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32 page(s)  
of draft labeling was  
redacted from the  
approval package