

19558\_5043

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPROVAL PACKAGE FOR:**

**APPLICATION NUMBER(S)**

**19-558/S-043**

**Trade Name:** Prinivil Tablets 2.5-, 5-, 10-, 20-,  
and 40 mg

**Generic Name(s):** (lisinopril)

**Sponsor:** Merck & Company

**Agent:**

**Approval Date:** May 29, 2003

**Indication:** Provides for proposed changes in the  
CLINICAL PHARMACOLOGY, WARNINGS, PRECAUTIONS,  
ADVERSE REACTIONS, and DOSAGE AND  
ADMINISTRATION sections of the labeling in pediatric  
patients

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RESEARCH**

**APPLICATION NUMBER:**

**19-558/S-043**

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**Reviews / Information Included in this NDA Review.**

<b>Approval Letter</b>	<b>X</b>
<b>Approvable Letter</b>	<b>X</b>
<b>Final Printed Labeling</b>	<b>X</b>
<b>Medical Review(s)</b>	<b>X</b>
<b>Chemistry Review(s)</b>	<b>X</b>
<b>EA/FONSI</b>	
<b>Pharmacology Review(s)</b>	
<b>Statistical Review(s)</b>	<b>X</b>
<b>Microbiology Review(s)</b>	<b>X</b>
<b>Clinical Pharmacology/ Biopharmaceutics Review(s)</b>	<b>X</b>
<b>Administrative Document(s)</b>	<b>X</b>
<b>Correspondence</b>	<b>X</b>

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**APPLICATION NUMBER**

**19-558/S-043**

**Approval Letter(s)**



NDA 19-558/S-043

Merck & Co., Inc.  
Attention: Jeffrey Tucker, M.D.  
Sumneytown Pike  
PO Box 4, BLA-20  
West Point, PA 19486

Dear Dr. Tucker:

Please refer to your supplemental new drug application dated September 24, 2001, submitted under section 505(b)/pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Prinivil (lisinopril) 2.5, 5, 10, 20 and 40 mg Tablets.

We acknowledge receipt of your submissions dated August 6, November 15 and December 27, 2002 and March 21 and May 14, 2003.

Your submission dated May 14, 2003 constituted a complete response to our July 25, 2002 action letter.

This supplemental new drug application proposes changes in the **CLINICAL PHARMACOLOGY, WARNINGS, PRECAUTIONS, ADVERSE REACTIONS, and DOSAGE AND ADMINISTRATION** sections of the labeling concerning the use of Prinivil (lisinopril) in pediatric patients.

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 May 14, 2003.

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  
5/29/03 09:41:35 PM

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**APPROVAL PACKAGE FOR:**

**APPLICATION NUMBER**

**19-558/S-043**

**Approvable Letter (S)**



NDA 19-558/S-043

Merck & Co., Inc.  
Attention: Michael C. Elia, Ph.D., DABT  
Sumneytown Pike  
P.O. Box 4, BLA-20  
West Point, PA 19486

Dear Dr. Elia:

Please refer to your September 24, 2001 supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prinivil (lisinopril) Tablet, 2.5, 5, 10, 20, and 40 mg.

We acknowledge receipt of your submissions dated November 19, 2001 and July 19, 2002.

This supplemental new drug application proposes changes in the **CLINICAL PHARMACOLOGY**, **PRECAUTIONS**, **ADVERSE REACTIONS**, and **DOSAGE AND ADMINISTRATION** sections of the labeling concerning the use of Prinivil 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.

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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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26 Page(s) Withheld

\_\_\_\_\_ § 552(b)(4) Trade Secret / Confidential

\_\_\_\_\_ § 552(b)(5) Deliberative Process

\_\_\_\_\_ § 552(b)(5) Draft Labeling