

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPLICATION NUMBER: NDA 19777/S15**

**CORRESPONDENCE**



# Pharmaceuticals Group

Stuart Pharmaceutical

NDA SUPPLEMENT  
SCM-015 (BC)

CERTIFIED MAIL  
RETURN RECEIPT REQUESTED

ICI Pharmaceuticals  
Group

Wilmington  
Delaware 19897 USA

Division of Cardio-Renal  
- Drug Products  
Center for Drug Evaluation and Research  
Food and Drug Administration  
HFD No. 110, Room No. 16B-30  
5600 Fishers Lane  
Rockville, MD 20857



Gentlemen:

AUG 31 1992

Re: ZESTRIL® (lisinopril)  
NDA 19-777  
ZESTORETIC® (lisinopril/hydrochlorothiazide)  
NDA 19-888

Pursuant to the August 28, 1992 conversation between Drs. Robert J. Wolters and James H. Short, of the Division of Cardio-Renal Drug Products, and Mr. Richard J. Pierce and Dr. Kevin McKenna, of ICI Pharmaceuticals Group, the lisinopril dihydrate synthesized at Macclesfield Works and imported into the United States for use in commercial drug product manufacture will be synthesized using either the

starting materials. The Agency approved the subject dipeptide starting materials and contract manufacturer for the manufacture of ZESTRIL® (lisinopril) Tablets (NDA 19-777) and ZESTORETIC® (lisinopril and hydrochlorothiazide) Tablets (NDA 19-888) on May 19, 1988 and July 20, 1989, respectively.

In addition to the two approved dipeptide starting materials listed in the preceding paragraph, the TFA-lisinopril ester alternative pivotal intermediate will also be used in the production of drug substance imported into the United States for the manufacture of commercial drug product. The Agency approved the use of the TFA-lisinopril ester pivotal intermediate for the manufacture of ZESTRIL Tablets (NDA 19-777) and ZESTORETIC Tablets (NDA 19-888) on November 9, 1990 and December 21, 1990, respectively.

Lisinopril dihydrate undergoing hydrogenation in the ZESTRIL Hydrogenation Plant (ZHP) provided for in the May 15, 1992 supplements to the subject NDAs will not be imported into the United States for commercial drug product manufacture until the ZHP receives a satisfactory current Good Manufacturing Practices inspection.

ORIGINAL

If you should require any further clarification or information, please do not hesitate to contact me.

Sincerely,

A handwritten signature in cursive script that reads "Kevin McKenna". The signature is written in dark ink and is positioned below the word "Sincerely,".

Kevin McKenna, Ph.D.  
Assistant Manager  
Technical Regulatory Affairs and Compliance  
Drug Regulatory Affairs Department  
(302) 886-2742

KM/mjb

Desk Copies: Dr. Robert J. Wolters, HFD No. 110, Room No. 16B-30  
Dr. James H. Short, HFD No. 110, Room No. 16B-30



# Pharmaceuticals Group

Stuart Pharmaceuticals/ICI Pharma

~~SUPPLY~~

**COPY 1**

HAND DELIVERED

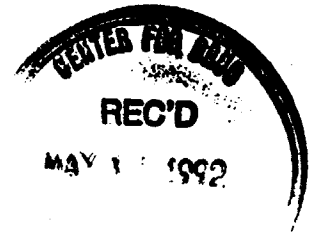
NDA NO. 19-777 REC. NO. 5-015  
NDA SUPPL FOR 5-015

**ICI Pharmaceuticals Group**

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Delaware 19897 USA

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MAY 15 1992



Gentlemen:

Re: ZESTRIL® (lisinopril) Tablets  
NDA 19-777  
ZESTORETIC® (lisinopril and hydrochlorothiazide) Tablets  
NDA 19-888

The purpose of this letter is to inform the Agency that the sponsor's Drug Master File (DMF), with information on the manufacturing, packaging and control of lisinopril dihydrate at its Macclesfield Works, Cheshire, England facilities was updated and submitted on May 15, 1992.

DMF can be identified as a Type submission, since the file includes information with respect to the facilities, personnel and general operating procedures, as well as manufacturing and quality control procedures.

The information contained in DMF is current as of this date, and will be kept current on an annual basis in accordance with the prescribed regulations.

The updated DMF is filed by Mr. Richard J. Pierce as the United States Agent for the file holder,

Mr. Richard J. Pierce  
Director  
Drug Regulatory Affairs  
ICI Americas Inc.  
Concord Pike and New Murphy Road  
Wilmington, DE 19897

**ORIGINAL**