

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
**75-909**

**CORRESPONDENCE**



DR. REDDY'S

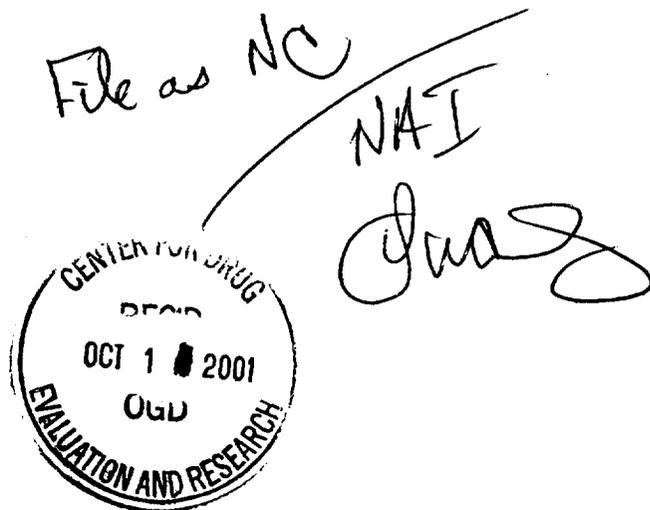
DR. REDDY'S LABORATORIES, INC.

ONE PARK WAY  
UPPER SADDLE RIVER, NJ 07458  
TELEPHONE (201) 760-2880  
FAX (201) 760-0401

September 26, 2001

Via Courier & Fax – 301 594-0108

Mr. Tim Ames, Project Manager  
Office of Generic Drugs  
Food and Drug Administration  
Document Control Room  
Center for Drug Evaluation and Research  
Metro Park North II  
7500 Standish Place, Room 150  
Rockville, MD 20855-2773



**RE: REQUEST FOR EXPEDITED REVIEW**  
**Enalapril Maleate and HCTZ Tablets USP, 5 mg/12.5 mg and 10 mg/25 mg.**  
**Dr. Reddy's Laboratories, Ltd./ANDA 75-909**

Dear Mr. Ames:

This request for expedited review is being submitted by the US Agent, Dr. Reddy's Laboratories, Inc. on behalf of Dr. Reddy's Laboratories Limited, Bachepalli, 502 325 India.

Further to my September 26<sup>th</sup>, teleconference with Mr. Gregory Davis-Branch Chief, we would like to make the agency aware of several inconsistencies with respect to the Agency's electronic "Orange Book" regarding the above referenced Drug Product.

On September 18, 2001, the Agency granted final approval status to several generic manufacturers of Enalapril Maleate and Hydrochlorothiazide based upon the expiration of US Patent 4,472,380. However, we would like to bring to your attention the 21st Edition of the *Approved Drug Products with Therapeutic Equivalence Evaluations* reflects a pediatric extension has been granted to Enalapril Maleate; Vasoretic, thus extending the exclusivity period to March 18, 2002 (Exhibit 1). Further, the most recent electronic update, *Cumulative Update No. 6*; indicates no deletions have been made to the published pediatric extension for Enalapril Maleate; Vasoretic (Exhibit 2).

In addition to these official publications, the Agency's website entitled *CDER New and Generic Drug Approvals* reflect its position that final approval shall be awarded upon the expiry of pediatric exclusivity ending on March 18, 2002, as reflected in several Tentative Approval Letters (Exhibit 3).

Page 2  
September 26, 2001  
Mr. Tim Ames, Office of Generic Drugs

Based upon this published literature, Dr. Reddy's Laboratories, Ltd. has justly assumed the granting of a full 6-months pediatric exclusivity period. Further, Dr. Reddy's Laboratories Ltd. had planned to maximize Drug Product expiration dating by strategically scheduling its validation batches and commercialization based upon the Agency's original posted position indicating a March 18, 2002 expiration of pediatric exclusivity. As a result of the Agency granting final approval prior to this dated, it would appear as though the Agency erroneously listed 6-months of pediatric exclusivity to Enalapril Maleate; Vasercetic (the '380 patent).

In consideration of the above commercial impact, Dr. Reddy's Laboratories, Inc. hereby requests an expedited review to its amendment submitted September 11, 2001 and for final approval to ANDA 75-909.

Should you have any questions to the request, please contact me at (201) 760-2880.

Very truly yours,

DR. REDDY'S LABORATORIES, INC.



Paul V. Campanelli  
Vice President, Formulations Business

cc. Mr. Gregory Davis, Office of Generic Drugs

Enclosures



ONE PARKWAY  
LITTLE LAMBDA ROAD, NORTH  
TELEPHONE: (201) 750-2880  
FAX: (201) 750-2401

HAND DELIVERED

September 28, 2001

Office of Generic Drugs  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Document Control Room  
Metro Park North II  
7500 Standish Place, Room 150  
Rockville, MD 20855-2773

ORIG AMENDMENT  
N/FA

**Reference: ANDA 75-909 Enalapril Maleate and Hydrochlorothiazide USP,  
5-12.5 mg and 10-25 mg**

**Telephone Amendment**

Dear Sir/ Madam:

This amendment is being submitted by the US Agent, Dr. Reddy's Laboratories, Inc. on behalf of Dr. Reddy's Laboratories Limited, Bachepalli, 502 325 India. Reference is made to the original submission dated June 16, 2000, the amendment submitted on March 28, 2001 and agency letters dated December 14, 2000, July 27, 2001 and September 11, 2001 and September 28, 2001. Reference is also made to the correspondence from Mr. Paul Campanelli dated September 27, 2001 relating to Pediatric Exclusivity being lifted.

**The agency request:**

*Please reduce the limits for the dimer present in the Hydrochlorothiazide from  
match the release limits.*

As requested the limits have been reduced. The Firm commits to provide revised copies of the specifications sheet to the agency.





Pursuant to *Code of Federal Regulations* Title 21 §314.440 (a) (4), a Field Copy of this application is being submitted to the Office of Generic Drugs. The Firm hereby certifies that it is a true copy of the technical section as described in *Code of Federal Regulations* Title 21 §314.50 (d) (1).

Please communicate any remaining questions or issues to C. Jeanne Taborsky, and they will be addressed and a response submitted immediately. This concludes our submission. Please feel free to contact me if you have any questions, tele (410) 309-3145, Fax (410) 309-6145.

Sincerely yours,

A handwritten signature in cursive script that reads "C. Jeanne Taborsky".

C. Jeanne Taborsky  
Regulatory Affairs





DR. REDDY'S

Dr. Reddy's Laboratories, Inc.

ONE PARK WAY  
UPPER SADDLE RIVER, NJ 07458  
TELEPHONE: (201) 760-2880  
FAX: (201) 760-0401

HAND DELIVERED

September 28, 2001

ORIG AMENDMENT

N/AA

Office of Generic Drugs  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Document Control Room  
Metro Park North II  
7500 Standish Place, Room 150  
Rockville, MD 20855-2773

Reference: **ANDA 75-909 Enalapril Maleate and Hydrochlorothiazide USP,  
5-12.5 mg and 10-25 mg**

**Gratuitous Labeling Amendment EXPEDITED**

Dear Sir/ Madam:

This amendment is being submitted by the US Agent, Dr. Reddy's Laboratories, Inc. on behalf of Dr. Reddy's Laboratories Limited, Bachepalli, 502 325 India. Reference is made to the original submission dated June 16, 2000, the amendment submitted on March 28, 2001 and agency letters dated December 14, 2000, July 27, 2001 and September 11, 2001.

Reference is also made to the correspondence from Mr. Paul Campanelli dated September 27, 2001 relating to Pediatric Exclusivity being lifted. Please be advised that the computer generated insert is of lesser quality than the actual insert. The US Agent commits to provide copies of the actual printed insert on receipt, next week.

The Firm is herein providing copies of computer generated final print labeling, and requesting immediate review and approval, should all chemistry issues be found to be satisfactory. Please communicate any remaining questions or issues to C. Jeanne Taborsky, and they will be addressed and a response submitted immediately. This concludes our submission. Please feel free to contact me if you have any questions, tele (410) 309-3145, Fax (410) 309-6145.

Sincerely yours,

C. Jeanne Taborsky  
Regulatory Affairs



FA noted, -  
to CMC Renewer for  
review.  
JRS  
9/14/01



**DR. REDDY'S**  
Dr. Reddy's Laboratories, Inc.

ONE PARK WAY  
UPPER SADDLE RIVER, NJ 07458  
TELEPHONE: (201) 760-2880  
FAX: (201) 760-0401

VIA FEDERAL EXPRESS  
September 11, 2001

Office of Generic Drugs  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Document Control Room  
Metro Park North II  
7500 Standish Place, Room 150  
Rockville, MD 20855-2773

N/FA  
OTIC AMENDMENT

Reference: **ANDA 75-909 Enalapril Maleate and Hydrochlorothiazide USP,  
5-12.5 mg and 10-25 mg**

**RESPONSE TO MINOR NA LETTER**

Dear Sir/ Madam:

This response is being submitted by the US Agent, Dr. Reddy's Laboratories, Inc. on behalf of Dr. Reddy's Laboratories Limited, Bachepalli, 502 325 India. Reference is made to the original submission dated June 16, 2000, the amendment submitted on March 28, 2001 and agency letters dated December 14, 2000 and July 27, 2001. The following information is the Firm's response to the agency CMC and Labeling questions:

FDA Comment:

A. *Chemistry Deficiencies:*

- 1.



Page (s) 1

Contain Trade Secret,  
Commercial/Confidential  
Information and are not  
releasable.

9/11/01

**B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comment in your response:**

*You have not yet responded to the labeling deficiencies communicated to you on December 14, 2001. The labeling for your drug product must be found acceptable in final print prior to approval.*

We note and acknowledge agency's comment. The response to the labeling deficiency is submitted below.

***Labeling Deficiencies dated December 14, 2000***

***1. Container – Bottles of 100 and 1000 tablets***

*Please ensure that the established name and expression of strength are the prominent print on the label.*

As per the agency's recommendation the size of established name and strength are increased to improve the prominence on the label. A comparison is provided in Section IV and the draft labels are provided in Section V Labeling.

***2. Package Insert***

***a. General comments***

*Please note that USAN names are common nouns and should be treated as such in the text of labeling (i.e., lower case). Upper case may be used when the USAN name stands alone as on labels or in the title of the package insert*

As requested by the agency, the USAN name has been treated as the common name in the labeling text (i.e. lower case), except for the title where upper case is used.

***b. Title:***

*We encourage you to include "USP" in the established name of your drug product in this section.*

In the side panel, under the heading 'Each tablet contains' "USP" is added after Enalapril Maleate and Hydrochlorothiazide.



DR. REDDY'S

Dr. Reddy's Laboratories, Inc.

c. *Description*

*Third Paragraph first sentence –*

*With a molecular weight of 492.53 (replace "with" with "weight" and replaces 492.52" with 492.53")*

As per agency's recommendation under "Description", paragraph third, "with" is "weight" and "492.52" is changed to "492.53".

This concludes our response to the Minor NA Letter. Please feel free to contact me if you have any questions, tele (410) 309-3145, Fax (410) 309-6145.

Sincerely yours,

C. Jeanne Taborsky  
Regulatory Affairs



DR. REDDY'S

Dr. Reddy's Laboratories, Inc.

ONE PARK WAY

UPPER SADDLE RIVER, NJ 07458

TELEPHONE: (201) 760-2880

FAX: (201) 760-6491

HAND DELIVERED

September 28, 2001

Office of Generic Drugs  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Document Control Room  
Metro Park North II  
7500 Standish Place, Room 150  
Rockville, MD 20855-2773

ORIG AMENDMENT

N/FA

**Reference: ANDA 75-909 Enalapril Maleate and Hydrochlorothiazide USP,  
5-12.5 mg and 10-25 mg**

**Telephone Amendment**

Dear Sir/ Madam:

This amendment is being submitted by the US Agent, Dr. Reddy's Laboratories, Inc. on behalf of Dr. Reddy's Laboratories Limited, Bachepalli, 502 325 India. Reference is made to the original submission dated June 16, 2000, the amendment submitted on March 28, 2001 and agency letters dated December 14, 2000, July 27, 2001 and September 11, 2001 and September 28, 2001. Reference is also made to the correspondence from Mr. Paul Campanelli dated September 27, 2001 relating to Pediatric Exclusivity being lifted.

**The agency request:**

*Please reduce the limits for the dimer present in the Hydrochlorothiazide from  
, match the release limits.*

As requested the limits have been reduced. The Firm commits to provide revised copies of the specifications sheet to the agency.





DR. REDDY'S

Dr. Reddy's Laboratories, Inc.

Pursuant to *Code of Federal Regulations* Title 21 §314.440 (a) (4), a Field Copy of this application is being submitted to the Office of Generic Drugs. The Firm hereby certifies that it is a true copy of the technical section as described in *Code of Federal Regulations* Title 21 §314.50 (d) (1).

Please communicate any remaining questions or issues to C. Jeanne Taborsky, and they will be addressed and a response submitted immediately. This concludes our submission. Please feel free to contact me if you have any questions, tele (410) 309-3145, Fax (410) 309-6145.

Sincerely yours,

C. Jeanne Taborsky  
Regulatory Affairs



66 South Maple Avenue,  
Ridgewood, NJ 07450  
Phone: 201-444-4424  
Fax: 201-444-1456

VIA FEDERAL EXPRESS  
March 28, 2001

Office of Generic Drugs  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Document Control Room  
Metro Park North II  
7500 Standish Place, Room 150  
Rockville, MD 20855-2773

ORIG AMENDMENT  
AC

Reference: **ANDA 75-909 Enalapril Maleate and Hydrochlorothiazide USP,  
5-12.5 mg and 10-25 mg  
RESPONSE TO MAJOR NA LETTER**



Dear Sir/ Madam:

Reference is made to the agency letter dated December 14, 2000. This response is being submitted by the US Agent, Reddy-Cheminor, Inc. on behalf of Dr. Reddy's Laboratories Limited, Bachepalli, 502 325 India. The following information is the agency CMC questions and the Firm's corresponding responses.

1. Regarding the active ingredient, Enalapril Maleate USP, we have the following Comments:

a. *Please tighten your specifications for, based upon observed values.*

The Specification of Organic Volatile Impurities and Residual Solvent have been revised to tighten the limits based on observed values. The revised specifications, and Analysis Report as per the revised specifications are provided in **Section VIII**.

b. *Please incorporate the test for Related Substances into the retest schedule.*

As recommended by the agency, the test for Related Substance is incorporated in Retest Schedule. The revised retest schedule is provided in **Section VIII**.

c. *Please revise your specifications for Related Impurities and incorporate a limit for the RSS isomeric impurity of Enalapril Maleate. Please specify limits that are bases upon observed values.*

The specifications are revised to incorporate a limit for RSS isomeric impurity. The revised specification for Related Impurities is well below the limits given in the monograph of Enalapril Maleate, USP in the USP 24, Supplement 3 (Page No. 3024). The existing test method for Related Substance is not resolving RSS isomeric impurity. Hence, USP 24, Supplement 3 test method is adopted with minor changes and the method is validated. The method validation of Related Substance is performed by API manufacturer (Dr. Reddy's Laboratories Limited - Bulk Drug Division) and the same method is transferred to Dr. Reddy's Laboratories Limited - Generic Division (Formerly Cheminor Drugs Limited - Pharma Division). The revised Specification and Analysis Report as per the revised specification are provided in **Section VIII** and the revised Test Procedures, Method Validation Report and Method Transfer Report are provided in **Section XV**.

- d. *Please provide a methods validation report for Related Substances (HPLC) and OVI/Residual Solvents (GC) according to the USP 24 General Chapter <1225> Validation of Compendial Methods of the CDER Guideline. Based upon the method's accuracy, please incorporate relative response factors, if known, into your calculation of known impurities.*

The method validation for Related Substance and Residual Solvents are performed according to USP 24 General Chapter <1225>. The method validation report for Related Substance is provided in **Section XV**, the method validation for Residual solvents was performed by API manufacturer (Dr. Reddy's Laboratories Limited - Bulk Drug Division) and the same method is transferred to Dr. Reddy's Laboratories Limited - Generic Division. The Method Transfer Report for Residual Solvents was already submitted in ANDA (Please refer to page no. 5205 - 5207). The method validation report for Residual Solvents is provided in **Section XV**. The Test Procedure is revised to incorporate relative response factor in the calculation of known impurities. The revised test procedure is provided in **Section XV**.

2. Regarding the active ingredient, Hydrochlorothiazide USP, we have the following comments:

- a. *Please incorporate a test for melting point, please specify a range based upon observed values.*

The specifications are revised to incorporate Melting range based on the observed values. The revised specifications and Analysis Report are provided in **Section VIII**.

- b. *Please provide a method validation report for Related Substance . Based upon the method's accuracy, please incorporate a relative response factor, if known, into your calculation of dimer impurity.*

~~Keeping the FDA comment (Point No. 2c) in view, the test method for estimation of \_\_\_\_\_ is changed. The \_\_\_\_\_ impurity standard is isolated and the method validation for estimation of \_\_\_\_\_ impurity is performed. The relative response factor is established and the test procedure is revised to incorporate, the relative response factor in the calculation of~~

Page (s) 4

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Information and are not

releasable.

3/28/07

We acknowledge the receipt of labeling deficiency and the response will be sent to labeling review branch separately, as labeling amendment.

We appreciate your assistance in this matter. Please feel free to contact me if you have any questions, tele (201) 444-4424, Fax (210) 444-1456.

Sincerely yours,

A handwritten signature in cursive script, appearing to read "Paul Campanelli".

Paul Campanelli  
Vice President

ONE PARK WAY  
UPPER SADDLE RIVER, NJ 07458  
TELEPHONE (201) 760-2880  
FAX (201) 760-0401

AUG 21 2001

SENT VIA FEDERAL EXPRESS

NEW CORRESP

NC

NA3 10/15/01  
Zak's team

Office of Generic Drugs  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Document Control Room  
Metro Park North II  
7500 Standish Place, Room 150  
Rockville, MD 20855-2773

Reference: **ANDA #75-909 Enalapril Maleate and Hydrochlorothiazide Tablets  
USP 5/12.5 mg and 10/25 mg  
Correspondence**

Dear Sir/ Madam:

Dr. Reddy's Laboratories, Inc. US Agent for Dr. Reddy's Laboratories Limited, Bachepalli 502 325, INDIA, is herein submitting a revised Letter of Authorization for US Agent with updated information.

Please be advised that the name and address of the US agent has changed.

Pursuant to *Code of Federal Regulations* Title 21 §314.440 (a) (4), a third copy of this communication is being provided. This is the required field copy and we certify that it is a true copy of the technical section as described in *Code of Federal Regulations* Title 21 §314.50 (d) (1).

This concludes our submission. Please contact C. Jeanne Taborsky at (410) 309-3145 or Paul V. Campanelli, Vice President Formulations Business, Reddy-Cheminor, Inc. at (201) 760-2880 ext 203, if you have any questions concerning this submission.

Sincerely yours,

*C. Jeanne Taborsky*  
C. Jeanne Taborsky  
Regulatory Affairs Consultant



66 South Maple Avenue,  
Ridgewood, NJ 07450

Phone: 201-444-4424  
Fax: 201-444-1456

**NEW CORRESP**

NC

January 16, 2001

Office of Generic Drugs  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Document Control Room  
Metro Park North II  
7500 Standish Place, Room 150  
Rockville, MD 20855-2773

**Reference: ANDA 75-909 Enalapril Maleate and Hydrochlorothiazide Tablets USP,  
5/12.5 and 10/25 mg  
Correspondence**

This correspondence is being provided by the US Agent on behalf of Cheminor Drugs Limited (Pharma Division), Via IDA Bollaram, Bachepalli - 502 325, INDIA. On January 2, 2001, the Andhra Pradesh High Court ruled on the merger of Cheminor Drugs Limited and Dr. Reddy's Laboratories. As of that date, Cheminor Drugs Limited is known as Dr. Reddy's Laboratories Limited.

The address and all other information remain the same. Documents have been filed to change the Registration Number and labeler code to that of Dr. Reddy's Laboratories Limited.

Pursuant to Code of Federal Regulations Title 21 § 314.440 (a) (4), a Field Copy of this correspondence is being submitted to the Office of Generic Drugs. The Firm hereby certifies that it is a true copy of the technical section as described in 21 CFR 314.50 (d) (1).

Thank you for your assistance in this matter. Please feel free to contact us if necessary.

Sincerely yours,

  
C. Jeanne Taborsky  
Regulatory Affairs Consultant



1/1 Duplicate

REDDY-CHEMINOR, INC. **R-C**

66 South Maple Avenue,  
Ridgewood, NJ 07450

Phone: 201-444-4424  
Fax: 201-444-1456

**NEW CORRESP**

NC

January 16, 2001

Office of Generic Drugs  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Document Control Room  
Metro Park North II  
7500 Standish Place, Room 150  
Rockville, MD 20855-2773

Acknowledged.  
B. notify HFD-92  
FBI/DOH 1/19/01

**Reference: ANDA 75-909 Enalapril Maleate and Hydrochlorothiazide Tablets USP,  
5/12.5 and 10/25 mg  
Correspondence**

This correspondence is being provided by the US Agent on behalf of Cheminor Drugs Limited (Pharma Division), Via IDA Bollaram, Bachepalli - 502 325, INDIA. On January 2, 2001, the Andhra Pradesh High Court ruled on the merger of Cheminor Drugs Limited and Dr. Reddy's Laboratories. As of that date, Cheminor Drugs Limited is known as Dr. Reddy's Laboratories Limited.

The address and all other information remain the same. Documents have been filed to change the Registration Number and labeler code to that of Dr. Reddy's Laboratories Limited.

Pursuant to Code of Federal Regulations Title 21 § 314.440 (a) (4), a Field Copy of this correspondence is being submitted to the Office of Generic Drugs. The Firm hereby certifies that it is a true copy of the technical section as described in 21 CFR 314.50 (d) (1).

Thank you for your assistance in this matter. Please feel free to contact us if necessary.

Sincerely yours,

*C. Jeanne Taborsky*  
C. Jeanne Taborsky  
Regulatory Affairs Consultant



66 South Maple Avenue  
Ridgewood, New Jersey 07450  
Telephone (201) 444-4424  
Telefax (201) 444-1456

September 20, 2000

Office of Generic Drugs  
Center for Drug Evaluation and Research  
Food and Drug Administration  
Document Control Room  
Metro Park North II  
7500 Standish Place, Room 150  
Rockville, MD 20855-2773

**NDA ORIG AMENDMENT**

N/AB

Reference: Telephone Amendment/Cheminor Drugs Limited  
Enalapril Maleate Tablets HCTZ/ANDA 75-909

Dear Sir or Madam:

On September 7, 2000, Reddy-Cheminor, Inc., (US Agent for Cheminor Drugs Ltd.) was contacted by Jennifer Fan and Patrick Nwakama from the Office of Generic Drugs regarding the above referenced ANDA 75-909.

Upon completion of the teleconference, the Sponsor was issued Telephone Amendment status for the following cited bioequivalence deficiencies:

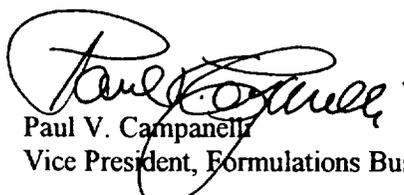
- Preliminary review of ANDA 75-909 was discussed. Issue: Reviewer can not locate percent recovery for the internal standards for  
• Reddy-Cheminor is required to provide data within 10 business days in order to maintain telephone amendment status.

Reddy-Cheminor herewith provides the following information via facsimile and hardcopy original:

- Determination of Hydrochlorothiazide in human Plasma by
- Determination of Enalapril and Enalaprilat in Human Plasma by .....

Please contact the undersigned at (201) 444-4424 or by fax at (201) 444-1456 should you have any questions regarding this submission.

Very truly yours,  
REDDY-CHEMINOR, INC.

  
Paul V. Campanelli  
Vice President, Formulations Business



Attachments

ANDA 75-909

Reddy-Cheminor, Inc.,  
U.S. Agent for: Cheminor Drugs Limited  
Attention: Paul V. Campanelli  
66 South Maple Avenue  
Ridgewood, NJ 07450  
|||||

AUG -9 2000

Dear Sir:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

NAME OF DRUG: Enalapril Maleate and Hydrochlorothiazide Tablets  
USP, 5 mg;12.5 mg and 10 mg;25 mg

DATE OF APPLICATION: June 16, 2000

DATE (RECEIVED) ACCEPTABLE FOR FILING: June 23, 2000

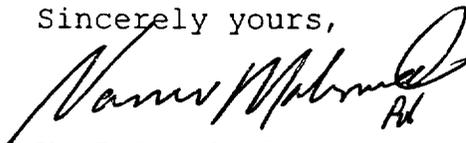
We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Bonnie McNeal  
Project Manager  
(301) 827-5848

Sincerely yours,



Wm Peter Rickman  
Acting Director  
Division of Labeling and Program Support  
Office of Generic Drugs  
Center for Drug Evaluation and Research

66 South Maple Avenue  
Ridgewood, New Jersey 07450  
Telephone (201) 444-4424  
Telefax (201) 444-1456

June 16, 2000

**Office of Generic Drugs**

Center for Drug Evaluation and Research  
Food and Drug Administration  
Document Control Room  
Metro Park North II  
7500 Standish Place, Room 150  
Rockville, MD 20855-2773

**Reference :**            **Enalapril Maleate and Hydrochlorothiazide Tablets, USP**  
                                 **5-12.5 mg and 10-25 mg.**  
                                 **Abbreviated New Drug Application**

Dear Sir/ Madam:

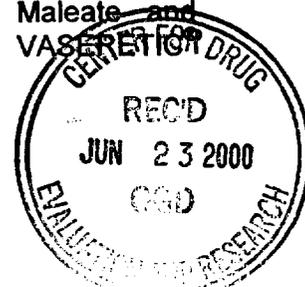
Cheminor Drugs Limited herewith submits an abbreviated new drug application (ANDA) for Enalapril Maleate and Hydrochlorothiazide Tablets, USP 5-12.5 mg and 10-25 mg pursuant to Section 505 (j) of the Federal Food, Drug, and Cosmetic Act.

This ANDA refers to the listed drug, VASERETIC® (Enalapril Maleate – Hydrochlorothiazide) Tablets, 5-12.5 mg and 10-25 mg which is manufactured by MERCK & Co., the holder of the approved application, and which is listed in the 1999 Approved Drug Products with Therapeutic Equivalence Evaluations, 19<sup>th</sup> Edition. U.S Patent No. 4,374,829 will expire on February 22, 2000 and patent number 4,472,380 will expire on September 18, 2001. Cheminor Drugs Limited is not seeking to market the product until after the patents expire.

Enalapril Maleate and Hydrochlorothiazide Tablets, USP 5-12.5 mg and 10-25 mg will be manufactured, tested and packed by at Cheminor Drugs Limited, Pharma Division, Bachepally, Post Bag No.: 15, Kukatpally P.O., Hyderabad – 500 072, INDIA in accordance with 21 CFR § parts 210 and 211.

Enalapril Maleate, USP manufactured by Dr. Reddy's Laboratories Limited, Plot No. 116, I.D.A. Bollaram, Narsapur (Tq), Medak (Dt.), Andhra Pradesh, INDIA, (DMF No. 13836), and Hydrochlorothiazide, USP manufactured by

The required bioavailability / bioequivalence studies were conducted on Enalapril Maleate and Hydrochlorothiazide Tablets, USP 10-25 mg and VASERETIC® (Enalapril Maleate – Hydrochlorothiazide) Tablets, 10-25 mg by AAI, 6101 Quadrangle Drive, Chapel Hill, NC 27514. These studies indicate that Enalapril Maleate and Hydrochlorothiazide Tablets, USP 10-25 mg are bioequivalent to VASERETIC® (Enalapril Maleate – Hydrochlorothiazide) Tablets, 10-25 mg.



# REDDY-CHEMINOR, INC.

June 16, 2000

Food and Drug Administration  
Enalapril Maleate and Hydrochlorothiazide Tablets, USP 5-12.5 mg and 10-25 mg.  
Abbreviated New Drug Application

Page 2

The *in-vitro* dissolution profiles for Enalapril Maleate and Hydrochlorothiazide Tablets, USP 5-12.5 mg and 10-25 mg are comparable to those of VASERETIC® (Enalapril Maleate – Hydrochlorothiazide) Tablets, 5-12.5 mg and 10-25 mg.

Enalapril Maleate and Hydrochlorothiazide Tablets, USP 5-12.5 mg and 10-25 mg are stable and a two year expiration dating is requested. The two year expiration dating for this product is supported by one, two and three months accelerated stability data (40°C / 75% relative humidity) in the smallest and largest package size of the container / closure system proposed for marketing. The stability studies were conducted under a stability protocol that is in conformance with the current FDA stability guidelines.

The dosage form, route of administration, active ingredient, potency and labeling (except DESCRIPTION and HOW SUPPLIED Sections) for Enalapril Maleate and Hydrochlorothiazide Tablets, USP 5-12.5 mg and 10-25 mg are the same as those for VASERETIC® (Enalapril Maleate–Hydrochlorothiazide) Tablets, 5-12.5 mg and 10-25 mg.

This ANDA is submitted in ten (10) volumes :

Volume I	:	Sections I through Section VI
Volume II	:	Section VI (continued)
through	:	
Volume VII	:	Section VI (continued) through Section VII
Volume VIII	:	Section VIII through Section XI
Volume IX	:	Section XII through Section XIV
Volume X	:	Section XV through Section XXII

Par Pharmaceutical, Inc. will be the distributor for this product. The proposed labeling has been prepared using the Par logo. A letter authorizing Reddy-Cheminor, Inc., to act as the U.S agent for this ANDA, is provided in Section XX. Included in this submission is an extra copy of our cover letter. Please acknowledge by date stamping this letter upon receipt and forwarding this copy to us in the self-addressed stamped envelope provided for your convenience.

**REDDY-CHEMINOR, INC.**

June 16, 2000

Food and Drug Administration  
Enalapril Maleate and Hydrochlorothiazide Tablets, USP 5-12.5 mg and 10-25 mg  
Abbreviated New Drug Application

Page 3

Pursuant to 21 CFR 314.440 (a) (4), a third copy of this application is also enclosed. This is the required field copy and we certify that it is a true copy of the technical section as described in 21 CFR 314.50 (d) (1).

Sincerely,

A handwritten signature in black ink, appearing to read "Paul V. Campanelli". The signature is written in a cursive style with a horizontal line underneath.

**Paul V Campanelli**  
Vice President  
Formulations Business