CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 19777/S31

CORRESPONDENCE

ORIGINAL COPY #1

ZENECA
Pharmaceuticals
A Business Unit of Zeneca Inc.

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

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

SEP 10 1996

Dr. Robert J. Wolters
Supervisory Chemist
Division of Cardio-Renal
Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration
HFD No. 110, Room No. 5066
Woodmont Office Complex 2
1451 Rockville Pike
Rockville, MD 20852

NDA SUPPL AMEND
SCP-031
(BC)

Dear Dr. Wolters:

Re: SORBITRATE® (isosorbide dinitrate) Chewable Tablets 5 mg
NDA 16-776
SORBITRATE® (isosorbide dinitrate) Oral Tablets 5 mg and 10 mg
NDA 16-192

TENORETIC® (atenolol and chlorthalidone) 25/12.5 mg, 50/25 mg and 100/25 mg
NDA 18-760
TENORMIN® (atenolol) Tablets 25 mg, 50 mg and 100 mg
NDA 18-240
ZESTORETIC® (lisinopril and hydrochlorothiazide) Tablets 10/12.5 mg, 20/12.5 mg, 10/25 mg and 20/25 mg
NDA 19-888
ZESTRIL® (lisinopril) Tablets 2.5 mg, 5 mg, 10 mg, 20 mg and 40 mg
NDA 19-777

The purpose of this submission is to amend our earlier supplemental New Drug Applications introducing an induction seal closure to the above noted products. Attached please find the Zeneca acceptance criteria for the induction seal component.

If you require any additional information, please do not hesitate to call.

RECEIVED
SEP. 16 1996
GENERIC DRUGS

Sincerely,

Norbert R. Ealer
Senior Regulatory Specialist, Marketed Products Group
Drug Regulatory Affairs Department
(302) 886-7633
(302) 886-2822 (fax)

NRE/lmc/4626/93
Enclosures

ORIGINAL

ZENECA
Pharmaceuticals
A Business Unit of Zeneca Inc.

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

JUN 18 1996

HAND DELIVERED

Dr. Robert J. Wolters
Supervisory Chemist
Center for Drug Evaluation and Research
Food and Drug Administration
HFD No. 110, Room No. 5066
Woodmont Office Complex 2
1451 Rockville Pike
Rockville, MD 20852

COPY 1

NDA NO. 19-777 REF. NO. 1

NDA SUPPL FOR 30

Dear Dr. Wolters:

Re: SORBITRATE® (isosorbide dinitrate) Chewable Tablets 5 mg
NDA 16-776

SORBITRATE® (isosorbide dinitrate) Oral Tablets 5 mg & 10 mg
NDA 16-192
TENORETIC® (atenolol and chlorthalidone) Tablets 25/12.5 mg, 50/25 mg & 100/25 mg
NDA 18-760
TENORMIN® (atenolol) Tablets 25 mg, 50 mg & 100 mg
NDA 18-240
ZESTRIL® (lisinopril) Tablets 2.5 mg, 5 mg, 10 mg, 20 mg & 40 mg
NDA 19-777
ZESTORETIC® (lisinopril & hydrochlorothiazide) Tablets 10/12.5 mg, 20/12.5 mg, 10/25 mg & 20/25 mg
NDA 19-888

The purpose of this submission is to provide the Agency information in support of the implementation of a tamper evident induction seal on the above dry oral solid dosage products currently manufactured by Zeneca.

The products affected by these changes are listed in Exhibit 1.

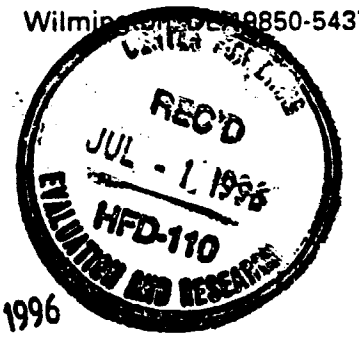
Exhibit 2 outlines the procedures, data and results of the analyses on the bottle/cap with a tamper evident inner seal. An analysis of heat transfer observed during the induction sealing process of the proposed bottle/cap configurations is also included.

ORIGINAL

ZENECA
Pharmaceuticals
A Business Unit of Zeneca Inc.

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

COPY #1



CERTIFIED MAIL
RETURN RECEIPT REQUESTED

JUN 2 5 1996

Dr. Robert J. Wolters
Supervisory Chemist
Division of Cardio-Renal
Drug Products
Center for Drug Evaluation and Research
Food and Drug Administration
HFD No. 110, Room No. 5066
Woodmont Office Complex 2
1451 Rockville Pike
Rockville, MD 20852

Dear Dr. Wolters:

Re: SORBITRATE® (isosorbide dinitrate) Chewable Tablets 5 mg
NDA 16-776 ✓
SORBITRATE® (isosorbide dinitrate) Oral Tablets 5 mg and 10 mg
NDA 16-192 ✓

TENORETIC® (atenolol and chlorthalidone) Tablets 25/12.5 mg, 50/25 mg and 100/25 mg
NDA 18-760 ✓
TENORMIN® (atenolol) Tablets 25 mg, 50 mg and 100 mg
NDA 18-240 ✓
ZESTORETIC® (lisinopril & hydrochlorothiazide) Tablets 10/12.5 mg, 20/12.5 mg, 10/25 mg and 20/25 mg
NDA 19-888 ✓
ZESTRIL® (lisinopril) Tablets 2.5 mg, 5 mg, 10 mg, 20 mg and 40 mg
NDA 19-777 ✓

The purpose of this submission is to provide the Agency with details of the stability matrix which we propose in support of the implementation of a tamper evident induction seal on the above dry oral solid dosage products currently manufactured by Zeneca. Strength/bottle presentations to be set down are denoted by an "X" in the following charts:

ORIGINAL

ZESTRIL TABLETS

STRENGTH>	5 mg	10 mg	20 mg	40 mg
BOTTLE				
100s	X	X	X	X
1000s	X		X	**********
3000s	**********	X		**********

ZESTORETIC TABLETS

STRENGTH>	10/12.5mg	20/12.5mg	20/25mg*
BOTTLE			
100s	X	X	

*This dosage strength is a double compression of the 10/12.5 mg dosage strength granulation and therefore, has been excluded from the test protocol.

SORBITRATE Chewable Tablets, 5 mg:

Set down 1 batch in the 100 tablet bottle.

SORBITRATE Oral Tablets, 5 mg and 10 mg:

Set down 1 batch of each strength in the 100 tablet bottle.

SORBITRATE Sublingual Tablets, 2.5 mg and 5 mg:

Set down 1 batch of each strength in the 100 tablet bottle.

TENORETIC TABLETS, 25/12.5 mg, 50/25 mg and 100/25 mg:

Set down 1 batch of each strength in the 100 tablet bottle.

TENORMIN TABLETS, 25 mg, 50 mg and 100 mg:

Set down 1 batch of each strength in the 100 tablet bottle.

Our submission of June 12, 1996 contained a list of all product dosage strengths and packages marketed for these products. A copy of that list is attached as Exhibit 1.

Exhibit 2 reflects our stability commitment.

Sincerely,

Robert Castor
Manager, Marketed Products Group
Drug Regulatory Affairs Department
(302) 886-2594
(302) 886-2822 (fax)

RC/NRE/jr/4428/91
Enclosures