

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1 !
 !
 IND # _____ YES /___/ ! NO /___/ Explain: _____
 !
 ! _____

Investigation #2 !
 !
 IND # _____ YES /___/ ! NO /___/ Explain: _____

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1 !
 !
 YES /___/ Explain _____ ! NO /___/ Explain _____
 !
 ! _____
 ! _____

Investigation #2 !
 !
 YES /___/ Explain _____ ! NO /___/ Explain _____
 !
 ! _____
 ! _____

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES / / NO / /

If yes, explain: _____

 / S /

Signature
Title: Project Manager

 8/2/99
Date

APPEARS THIS WAY
ON ORIGINAL

 / S /

Signature of Office/
Division Director

 8-4-99
Date

cc: Original NDA Division File HFD-93 Mary Ann Holovac

APPEARS THIS WAY
ON ORIGINAL



hvc
human health care

Eisai, Inc.
Glenpointe Centre West
400 Frank W. Burr Blvd.
Teaneck, New Jersey 07666
Telephone: 201 692-9160
Fax: 201 692-9183

BEST POSSIBLE COPY

August 2, 1999

Lilia Talarico, M.D., Director
Division of Gastrointestinal and
Coagulation Drug Products, HFD-180
Food and Drug Administration
Center for Drug Evaluation and Research
Attention: Division Document Room, 6B-24
5600 Fischers Lane
Rockville, Maryland 20857

RE: NDA# 20-973 – Response to Request for Information
PRODUCT: Aciphex™ (rabeprazole sodium) 20mg delayed-release tablets

Dear Doctor Talarico:

Reference is made to our original drug application for Aciphex (rabeprazole sodium).

Eisai, Inc. hereby requests a five (5) year period of exclusivity for rabeprazole sodium in accord with sections 505(j)(4)(D)(iii) and 505 (C)(3)(3)(D)(ii) of the Federal Food, Drug, and Cosmetic Act in that the active ingredient, rabeprazole sodium has not been approved in any other New Drug Application in the United States.

Should you have any questions or require additional information, please do not hesitate to contact me at 201 287 2120.

Sincerely,
EISAI INC.

Kathryn Bishburg, Pharm.D.
Executive Director, Regulatory Affairs



hke
human health care

Eisai Inc.
Regulatory Affairs Dept.
Glenpointe Centre West
500 Frank W. Burr Blvd.
Teaneck, New Jersey 07666
Telephone: 201 692-9160
Fax: 201-287-1409

January 22, 1999

Lilia Talarico, M.D.
Director
Division of Gastrointestinal and
Coagulation Drug Products, HFD-180
Food & Drug Administration
Center for Drug Evaluation and Research
Attention: Document Control Room 6B-24
5600 Fishers Lane, Parkway Building
Rockville, MD 20852-1706

BEST POSSIBLE COPY

**Subject: NDA 20-973 – Aciphex™ (rabeprazole sodium) Tablets
Response to FDA Request for Additional Information**

Dear Dr. Talarico:

We are responding to the telephone request of January 14, 1999 by Mr. Brian Strongin of your Division concerning the original Debarment Certification submitted with the subject NDA.

Please find enclosed a revised Debarment Certification for the subject NDA that has been signed by Eisai Inc.'s Vice President of Clinical Research.

We believe that the foregoing is responsive to your request. Please let me know if you have any questions at your earliest convenience.

Please be advised that material and data contained in this submission are confidential. The legal protection of such confidential material is hereby claimed under applicable provisions of 18 U.S.C., Section 1905 or 21 U.S.C., Section 331 (J).

Sincerely,

Megan M. Parsi
Manager, Regulatory Affairs

MMP/mm
Encl.

Submission in Duplicate

Debarment Certification
NDA 20-973

The Applicant, Eisai Inc., hereby certifies that it did not and will not use in any capacity the services of any person debarred under Section 306 (a) or (b) of the Generic Drug Enforcement Act of 1992 in connection with this application.

Eisai Inc.

By: 

William F. Hahne, MD.
Vice President, Clinical Research

1/22/93
Date

NDA 20-973

Debarment Certification

William F Hahne, M.D. hereby certifies that to the best of his knowledge and belief, he did not and will not use in any capacity the services of any person debarred under section 306(a) or (b) of the Generic Drug Enforcement Act of 1992 in connection with this application.



William F. Hahne, M.D.
Executive Director
Clinical Research
Eisai, Inc.

3/30/98
Date

CSO/Walsh

NDA 20-973

Eisai Inc.
Attention: Kathryn Bishburg, Pharm.D.
Glenpointe Centre West
500 Frank W. Burr Blvd.
Teaneck, N.J. 07666

MAR 12 1999

Dear Ms. Bishburg:

We acknowledge receipt on March 5, 1999 of your March 5, 1999 resubmission to your new drug application (NDA) for Aciphex (rabeprazole sodium) Delayed-Release Tablets.

This resubmission contains additional clinical, chemistry, and biopharmaceutical information submitted in response to our January 29, 1999 action letter.

We consider this a complete class 2 response to our action letter. Therefore, the user fee goal date is September 3, 1999.

If you have any questions, contact Maria R. Walsh, M.S., Regulatory Project Manager, at (301) 443-8017.

Sincerely,

 3-11-99

Lilia Talarico, M.D.
Director
Division of Gastrointestinal and Coagulation Drug
Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

CSO/Strongin

MEMORANDUM OF TELECON

DATE: October 28, 1998

APPLICATION NUMBER: NDA 20-973; Aciphex (rabeprazole sodium) Tablets

BETWEEN:

Name: Paul Manierre, Regulatory Affairs
Phone: (201) 287-2160
Representing: Eisai Inc.

AND

Name: Maria R. Walsh, Regulatory Project Manager
Division of Gastrointestinal and Coagulation Drug Products, HFD-180

SUBJECT: Request for endoscopy reports

TODAY'S CALL: I called Ms. Megan Parsi and spoke with Mr. Paul Manierre in her absence. Per Drs. Senior and Gallo-Torres (see text of e-mail below), I asked Mr. Manierre to provide the following: 1) all the endoscopy reports from the two European studies in GERD and GERD maintenance, namely, Studies H4M-MC-NRRP and H4M-MC-NRRQ; and 2) identification for which patients in the maintenance studies (H4M-MS-NRRQ, H4M-MC-NRRK-ODD, and H4M-MC-NRRK-EVEN) were healed on rabeprazole in the acute healing studies (H4M-MC-NRRI and H4M-NRRJ) and which were healed on another agent (specify) before entering the maintenance studies.

Mr. Manierre said the sponsor will provide the information and will call me with an estimate of time to response. The call was then concluded.

Attachment:

TO: Maria Walsh (WALSH)
CC: Brian Strongin (STRONGINB)
CC: Hugo Gallo Torres (GALLOTORRESH)
CC: Lilia Talarico (TALARICO)
Subject: Re: Rabeprazole

Maria,

1) Thank you for your quick action. Dr. Gallo-Torres and I have discussed this matter, and wish to request of the sponsor ALL of the endoscopy reports from the two European studies, referred to in the NDA 20-973 submission as Studies NRRP and NRRQ. Since there was another interim sponsor, Lilly, in addition to the submitting sponsor, Eisai, it

NDA 20-973

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is a little confusing since both put protocol numbers on each study.

Study "P" was carried out in 9 European countries, 27 investigators/202 patients, for healing of erosive lesions of GERD on either rabeprazole 20 mg/day (100 patients) or omeprazole 20 mg/day (102 patients). It is referred to in full as:

E3810-E044-307 and as H4M-MC-NRRP/LY307640 (Vol. 187-191/283)

The follow-up, maintenance of healing study, "Q", was carried out in 8 of the 9 countries (not Germany) by 21 of the same investigators (6 did not continue), on 243 patients randomized to rabeprazole 10 mg/day (82), rabeprazole 20 mg/day (78), or omeprazole 20 mg/day (83), for a year. Since only 189 of the 202 patients from Study "P" healed on rabeprazole or omeprazole and would have been available for "rollover" into Study "Q", it was necessary for the investigators to add at least 54 patients healed on other regimens. The full name of Study "Q" was:

E3810-E044-398 and H4M-MC-NRRQ/LY307640 (Vol. 210-216/283)

2) Separate issue, second request: In addition to requesting ALL of the endoscopy reports from both Study P and Q, it would be very helpful if the sponsor would provide identification for which patients in the maintenance Study Q had been healed on what agent before entering maintenance treatment. Previous work on duodenal ulcer healing and maintenance had shown that the agent used for healing affected greatly the tendency to relapse/recur, and this may be the case for erosive esophagitis. This linkage information is needed in order to do the maintenance data review. If the sponsor will provide this also for the linked North American studies NRRJ/NRRK for healing and the maintenance Study NRRKodd/even, it would speed the review. The full names for these North American studies, for which patient identification and linkage is requested, are:

Healing:

E3810-L001-203 a.k.a. H4M-MC-NRRI/LY307640 (Vol. 176-8/283)

E3810-A001-303 a.k.a. H4M-MC-NRRJ/LY307640 (Vol. 164-9/283)

Maintenance:

E3810-A001-304 a.k.a. H4M-MC-NRRK-ODD/LY307640 (Vol. 192-9/283)

E3810-A001-304 a.k.a. H4M-MC-NRRK-EVEN/LY307640 (Vol. 200-9)

NDA 20-973
Page 3

Many thanks,

JRS

/S/ 10/29/98

Maria R. Walsh, M.S.
Regulatory Project Manager

cc: Original NDA 20-973
HFD-180/Div. File
HFD-180/PM/B.Strongin
HFD-180/J.Senior
H.Gallo-Torres
L.Talarico

Final: M.Walsh
filename: 20973810.tel.doc

**APPEARS THIS WAY
ON ORIGINAL**

TELECON

C80/Walsh

MEMORANDUM OF TELECON

DATE: August 3, 1998

APPLICATION NUMBER: NDA 20-973; Aciphex (rabeprazole) Tablets

BETWEEN:

Name: Megan Parsi, Regulatory Affairs
Phone: (201) 287-2160
Representing: Eisai Inc.

AND

Name: Maria R. Walsh, M.S., Regulatory Project Manager
Division of Gastrointestinal and Coagulation Drug Products, HFD-180

SUBJECT: DMF References

TODAY'S CALL: Per the chemistry reviewer, Dr. Marie Kowblansky, I called Ms. Parsi and requested that the sponsor provide the submission dates for the items referenced in the Drug Master Files (DMFs). I told Ms. Parsi that I would fax to her today the list of DMF numbers and the corresponding referenced items (see attached). Ms. Parsi said she would provide the dates and the call was then concluded.

/S/ 8/8/98

Maria R. Walsh, M.S.
Regulatory Project Manager

cc: Original NDA 20-973
HFD-180/Div. File
HFD-180/PM/M. Walsh
HFD-180/M.Kowblansky
E.Duffy
Filename: 20973808.tel.doc

TELECON

