

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 020973

CHEMISTRY REVIEW(S)

DIVISION OF GASTROINTESTINAL AND COAGULATION DRUG PRODUCTS
Review of Chemistry, Manufacturing and Controls

NDA: 20-973

Chem. Review: #1

Review Date: 11/30/98

Submission Type
Original

Document Date
March 31, 1998
August 26, 1998

CDER Date
April 2, 1998

Assigned Date
April 27, 1998

DEC - 2 1998

Name and Address of Applicant:

Eisai, Inc.
Glenpointe Centre West
500 Frank W. Burr Blvd.
Teaneck, NJ 07666-6741

Drug Product Name:

Proprietary:-	ACIPHEX™ Tablets
Non-proprietary/USAN and CAS:	rabeprazole sodium
Code Number (CAS):	117976-90-6
Code Number (laboratory):	ER-3384
Chem. Type/Ther. Class	Proton Pump Inhibitor
Other Names:	Pariet™, SHKA, sodium pariprazole, E3810, <input type="text"/> 307640

ANDA Suitability Petition/DESI/Patent Status: N/A

Pharmacological Category /Indications:

-proton pump inhibitor
-treatment of DU, GERD, and GERD Maintenance and ZES

Dosage Form: Tablet, delayed release, enteric-coated

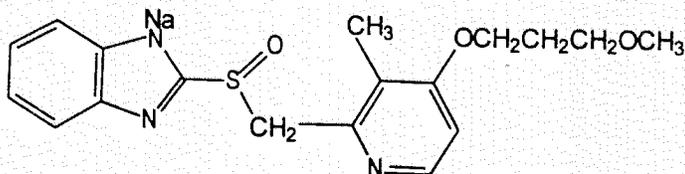
Strength: 10mg and 20mg

Route of Administration: oral

How Dispensed: Rx OTC

Chemical Name, Molecular Formula, Molecular Weight, Structural Formula

Chemical Name: 2-[[[4-(3-methoxypropoxy)-3-methyl-2-pyridyl]-methyl]sulfinyl]-1H-benzimidazole sodium salt
Structure:



Molecular Formula: C₁₈H₂₀N₃NaO₃S

Molecular Weight: 381.43

Supporting Documents

DMF NUMBER	SUBJECT	HOLDER	STATUS	REVIEW DATE	LETTE R DATE

Consults:

- Statistical stability review. See October 28, 1998, report from A. J. Sankoh, Ph.D.
- Biopharm. Review. See report from Carol Cronenberger, Ph.D.

Remarks/Comments

The applicant has good control of the manufacturing process, both for the bulk drug substance and the 20 mg tablets, as evidenced by the excellent batch to batch reproducibility of impurity and stability profiles (even when comparing full-scale and pilot batches).

For the 10 mg tablets, the stability data that were provided were inadequate to allow expiration dating with reasonable certainty.

APPEARS THIS WAY
ON ORIGINAL

Conclusions and Recommendations

From the CMC perspective, the 20 mg tablet is approvable with a 24 month expiration, pending resolution of the deficiencies listed in the draft letter.

Consideration of the approvability of the 10 mg tablet should be deferred until additional stability data have been provided and the ambiguity regarding the stability of the product is resolved.

/S/

Marie Kowblansky, PhD
Review Chemist, HFD-180

APPEARS THIS WAY
ON ORIGINAL

/S/

Eric P. Duffy, PhD
Chemistry Team Leader, HFD-180

cc: Orig. NDA 20-973
HFD-180/Division File
HFD-180/LTalarico/
DISTRICT OFFICE
HFD-180/CSO/BStrongin
HFD-820/JGibbs
HFD-180/EPDuffy
HFD-180/MKowblansky
R/D init.: Duffy/12-1-98
MK/dob F/T 12-2-98\ WORD: n:\wordfiles\chem\N\20973811.1MK

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ON ORIGINAL

DIVISION OF GASTROINTESTINAL AND COAGULATION DRUG PRODUCTS
Review of Chemistry, Manufacturing and Controls

NDA: 20-973

Chem. Review: #2

Review Date: 7/16/99

Submission Type

Document Date

CDER Date

Assigned Date

Amendment

March 5, 1999

March 5, 1999

March 10, 1999

Amendment

April 23, 1999

April 26, 1999

April 28, 1999

Name and Address of Applicant:

Eisai, Inc.
Glenpointe Centre West
500 Frank W. Burr Blvd.
Teaneck, NJ 07666-6741

JUL 23 1999

Drug Product Name:

Proprietary:

ACIPHEX™ Tablets

Non-proprietary/USAN and CAS:

rabeprazole sodium

Code Number (CAS):

117976-90-6

Code Number (laboratory):

ER-3384

Chem. Type/Ther. Class

Type 1S, New molecular Entity/Proton Pump Inhibitor

Other Names:

Pariet™, SHKA, sodium pariprazole, E3810, 307640

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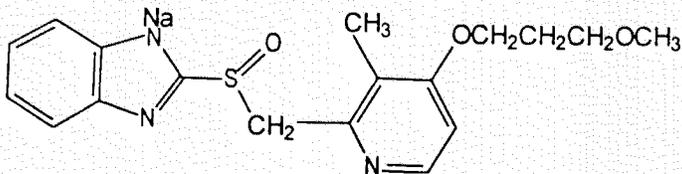
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How Dispensed: Rx OTC

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Molecular Weight: 381.43

Supporting Documents:

DMF NUMBER	SUBJECT	HOLDER	STATUS	REVIEW DATE	LETTER DATE
[REDACTED]					

Consults: Biophar.—review not completed

Remarks/Comments

Conclusions and Recommendations

From the CMC perspective, the 20 mg tablet is approvable with a 24 month expiration, pending resolution of the deficiencies listed in the draft letter.

[REDACTED] /S/ 7/23/99
Marie Kowblansky, PhD
Review Chemist, HFD-180

APPEARS THIS WAY
ON ORIGINAL

[REDACTED] /S/ 7/23/99
Eric P. Duffy, PhD
Chemistry Team Leader, HFD-180

- cc: Orig. NDA 20-973
- HFD-180/Division File
- HFD-180/LTalarico/
- DISTRICT OFFICE
- HFD-180/CSO/MWalsh
- HFD-820/JGibbs
- HFD-180/EPDuffy
- HFD-180/MKowblansky

APPEARS THIS WAY
ON ORIGINAL

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DIVISION OF GASTROINTESTINAL AND COAGULATION DRUG PRODUCTS
Review of Chemistry, Manufacturing and Controls

NDA: 20-973 Chem. Review: #3 Review Date: 7/28/99 AUG 4 1999
Submission Type Document Date CDER Date Assigned Date
Amendment July 26, 1999

Name and Address of Applicant:

Eisai, Inc.
Glenpointe Centre West
500 Frank W. Burr Blvd.
Teaneck, NJ 07666-6741

Drug Product Name:

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Non-proprietary/USAN and CAS:	rabeprazole sodium
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Code Number (laboratory):	ER-3384
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LY307640	

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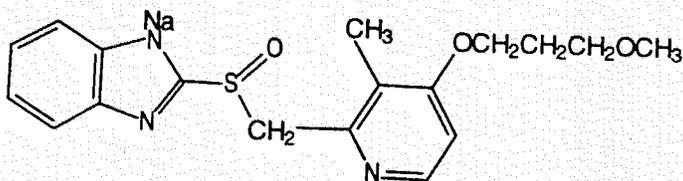
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