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  Document Date  CDER Date  Assigned Date
August 26, 1998

Name and Address of Applicant:
Eisai, Inc.
Glenpointe Centre West
500 Frank W. Burr Blvd.
Teaneck, NJ 07666-6741

Drug Product Name:
Proprietary: ACIPHEXTM 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: ParietTM, SHKA, sodium pariprazole, E3810, 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

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Consults:
- 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

/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
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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: Amendment
Document Date: March 5, 1999
CDER Date: March 5, 1999
Assigned Date: 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

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

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: 20mg
Route of Administration: oral

How Dispensed:  R x  OTC

Chemical Name, Molecular Formula, Molecular Weight, Structural Formula

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

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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.

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cc: Orig. NDA 20-973
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HFD-180/EPDuffy
HFD-180/MKowblansky

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/\S/ 7/23/99
Marie Kowblansky, PhD
Review Chemist, HFD-180

/\S/ 7/23/99
Eric P. Duffy, PhD
Chemistry Team Leader, HFD-180
DIVISION OF GASTROINTESTINAL AND COAGULATION DRUG PRODUCTS
Review of Chemistry, Manufacturing and Controls

Submission Type: Amendment
Document Date: July 26, 1999
CDER Date: Assigned Date

Name and Address of Applicant:
Eisai, Inc.
Glenpointe Centre West
500 Frank W. Burr Blvd.
Teaneck, NJ 07666-6741

Drug Product Name:
Proprietary: -
Non-proprietary/USAN and CAS: ACIPHEX™ Tablets
Code Number (CAS): rabeprazole sodium
Code Number (laboratory):
Chem. Type/Ther. Class
Type 1S, New molecular Entity/Proton Pump Inhibitor
Other Names:
LY307640

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: 20mg
Route of Administration: oral
How Dispensed: \( \sqrt{R} \), OTC

Chemical Name, Molecular Formula, Molecular Weight, Structural Formula

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

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Consults: Biopharm.— review not completed

Remarks/Comments
The applicant should be reminded that we have not yet received three copies of the Methods Validation Package.

Conclusions and Recommendations
From the CMC perspective, the 20 mg tablet should be approved with a 24 month expiration date.

/\S/ 8/3/99
Marie Kowblansky, PhD
Review Chemist, HFD-180

/\S/ 8/4/99
Eric P. Duffy, PhD
Chemistry Team Leader, HFD-180

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