

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

20988

CHEMISTRY REVIEW(S)

Related Documents: NDA 20-987

Supporting Documents

DMF	SUBJECT	DMF HOLDER	STATUS	REVIEW DATE	LETTER DATE
	Drug Substance Manufacturer	Byk Gulden	Deficient	4/2/99	2/4/99 4/5/99
	Rubber closure supplier		Adequate	5/13/99	---
	Glass vial supplier		Not reviewed*	---	---
	Glass vial supplier		Not reviewed*	---	---

*It is not our policy to review DMFs for USP glass containers.

Consults:

Biopharm. Review. See report from David Udo, Ph.D.

Sterility Review. Approval is recommended with regard to sterility assurance issues. See the microbiology review from Neal Sweeny, Ph.D.

Remarks/Comments

This product is manufactured for Wyeth-Ayerst by Byk-Gulden; the packaging and release testing is done at Wyeth-Ayerst. NDA 20-987 (Wyeth-Ayerst) for pantoprazole tablets was recently reviewed. Consequently, many of the chemistry issues that are common to NDAs 20-987 and 20-988 have not necessarily been documented here with the same degree of detail as in the former review. Issues specific to this dosage form have been highlighted in this review.

Conclusions and Recommendations

Insufficient information has been provided to demonstrate that the drug substance is a sesquihydrate (as claimed) and which hydrated form was used in clinical studies. However, since the drug is administered as a true solution, whether the drug substance is a monohydrate, sesquihydrate, etc. is immaterial to its biological activity. The NDA should be considered approvable once the issues cited in the deficiency letter are adequately addressed.

ISL
Marie Kowblansky, PhD
Review Chemist, HFD-180

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

5/14/99

5/14/99

cc: Orig. NDA 20-988
HFD-180/Division File
HFD-180/LTalarico
DISTRICT OFFICE
HFD-180/CSO/MWalsh
HFD-820/JGibbs
HFD-180/EPDuffy
HFD-180/Mkowblansky
R/D init./EDuffy/5-14-99
MK/dob F/T 5-14-99/ Word: n:\wordfiles\chem\N\20988905.MK

Redacted 14

pages of trade

secret and/or

confidential

commercial

information

Chemistry, Manufacturing and
Controls

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

NDA: 20-988

Chem. Review: #2

Review Date: 6/1/99

Submission Type
OriginalDocument Date
May 13, 1999CDER Date
May 17, 1999Assigned Date
May 18, 1999 JUN - 4 1999**Name and Address of Applicant:**

Wyeth Ayerst Laboratories
P.O. Box 8299
Philadelphia, PA 19101-8299

Drug Product Name:

Proprietary: PROTONIX™ I.V.
Non-proprietary/USAN and CAS: pantoprazole sodium sesquihydrate
Code Number (CAS): 138786-67-1
Code Number (laboratory): B8610-23, B8610-023 (Byk-Gulden)
WAY-140951 (Wyeth-Ayerst code)
Chem. Type/Ther. Class: ~~Type I~~, New Molecular Entity//Proton Pump Inhibitor
I/S

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

Pharmacological Category /Indications:

-proton pump inhibitor
-short term gastric acid suppression in GERD patients unable to take oral medication

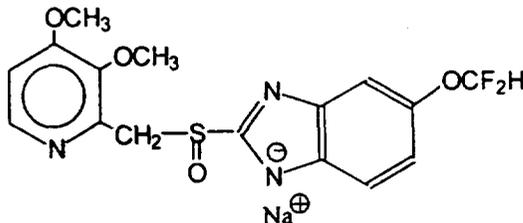
Dosage Form: lyophilized powder for reconstitution

Strength: 40 mg (pantoprazole) per vial

Route of Administration: intravenous

How Dispensed: Rx OTC**Chemical Name, Molecular Formula, Molecular Weight, Structural Formula****Chemical Name:**

Sodium-[5-(difluoromethoxy)-2-[(3,4-dimethoxy-2-pyridyl)-methyl]-sulfinyl]-1H-benzimidazole
sesquihydrate

Structure:Molecular Formula: C₁₆H₁₄F₂N₃NaO₄S x1.5 H₂O

Molecular Weight: 432.4 (includes water)

Consults: None

Remarks/Comments: See review.

Conclusions and Recommendations: The proposed labeling is unacceptable and should be modified as noted in the attached review.

ISR

Marie Kowblansky, PhD
Review Chemist, HFD-180

6/4/99

ISI

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

6/4/99

cc: Orig. NDA 20-988
HFD-180/Division File
HFD-180/LTalarico
DISTRICT OFFICE
HFD-180/CSO/MWalsh
HFD-820/JGibbs
HFD-180/EPDuffy
HFD-180/MKowblansky
c:\wordfiles\chem\N20988906.MK

Redacted 2

pages of trade

secret and/or

confidential

commercial

information

Chem. manufacturing + controls

Related Documents: NDA 20-987

Supporting Documents

DMF	SUBJECT	DMF HOLDER	STATUS	REVIEW DATE	LETTER DATE
	Drug Substance Manufacturer	Byk Gulden	Deficient	4/2/99	2/4/99 4/5/99 11/23/99
	Rubber closure supplier		Adequate	5/13/99	---
	Glass vial supplier		Not reviewed*	---	---
	Glass vial supplier		Not reviewed*	---	---

*It is not our policy to review DMFs for USP glass containers.

Consults:

Biopharm. Review. See report from David Udo, Ph.D.

Sterility Review. Approval is recommended with regard to sterility assurance issues. See the microbiology review from Neal Sweeny, Ph.D.

Remarks/Comments

This product is manufactured for Wyeth-Ayerst by Byk-Gulden; the packaging and release testing is done at Wyeth-Ayerst. NDA 20-987 (Wyeth-Ayerst) for pantoprazole tablets was recently reviewed. Consequently, many of the chemistry issues that are common to NDAs 20-987 and 20-988 have not necessarily been documented here with the same degree of detail as in the former review. Issues specific to this dosage form have been highlighted in this review.

Conclusions and Recommendations

The NDA is considered approvable (24 month expiration with storage at 2-8°C) once the remaining deficiencies are adequately addressed.

/S/ 12/14/99
Marie Kowblansky, PhD
Review Chemist, HFD-180

/S/ 12/14/99
Liang Zhou, PhD
Acting Chemistry Team Leader, HFD-180

cc: Orig. NDA 20-988
HFD-180/Division File
HFD-180/LTalarico
HFD-180/CSO/MWalsh
HFD-820/JGibbs
HFD-180/LZhou
HFD-180/MKowblansky
c:\wordfiles\chem\N20988912.MK

Redacted 7

pages of trade

secret and/or

confidential

commercial

information

Chem. manufacturing + controls

FEB - 7 2000

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

NDA: 20-988 Chem. Review: #4 Review Date: 2/3/00

Submission Type	Document Date	CDER Date	Assigned Date
BC	January 19, 2000	January 20, 2000	January 27, 2000
AC	August 31, 1999	September 1, 1999	
Original	July 20, 1998, 1998	July 22, 1998	

Name and Address of Applicant:

Wyeth Ayerst Laboratories
P.O. Box 8299
Philadelphia, PA 19101-8299

Drug Product Name:

Proprietary:	PROTONIX™
Non-proprietary/USAN and CAS:	pantoprazole sodium
Code Number (CAS):	164579-32-2
Code Number (laboratory):	B8610-23, B8610-023 (Byk-Gulden) WAY-140951 (Wyeth-Ayerst code)
Chem. Type/Ther. Class	Type IS

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

Pharmacological Category /Indications:

- proton pump inhibitor
- short term gastric acid suppression in GERD patients unable to take oral medication

Dosage Form: lyophilized powder for reconstitution

Strength: 40 mg (pantoprazole) per vial

Route of Administration: intravenous

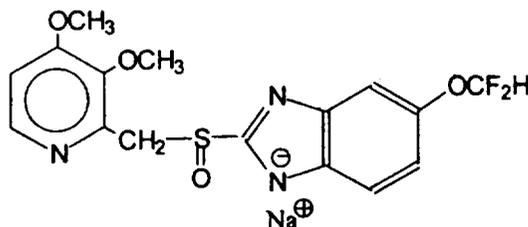
How Dispensed: Rx OTC

Chemical Name, Molecular Formula, Molecular Weight , Structural Formula

Chemical Name :

Sodium-[5-(difluoromethoxy)-2-[(3,4-dimethoxy-2-pyridyl)-methyl]-sulfinyl]-1H-benzimidazole sesquihydrate

Structure:



Molecular Formula: C₁₆H₁₄ F₂N₃NaO₄S x1.5 H₂ O

Molecular Weight: 432.4 (includes water)

Related Documents: NDA 20-987

Supporting Documents

DMF	SUBJECT	DMF HOLDER	STATUS	REVIEW DATE	LETTER DATE
	Drug Substance Manufacturer	Byk Gulden	Adequate	1/14/00	2/4/99 4/5/99 11/23/99
	Rubber closure supplier		Adequate	5/13/99	---
	Glass vial supplier		Not reviewed*	---	---
	Glass vial supplier		Not reviewed*	---	---

*It is not our practice to review DMFs for USP glass containers.

Consults:

Biopharm. Review. Approval is recommended. See report from David Udo, Ph.D.

Sterility Review. Approval is recommended with regard to sterility assurance issues. See the microbiology review from Neal Sweeny, Ph.D.

Remarks/Comments: See review

Conclusions and Recommendations

The NDA is considered approvable pending the submission of satisfactory admixture photostability data and compatibility information for the product with the admixture container.

ISI 2/7/00

Marie Kowblansky, PhD
Review Chemist, HFD-180

ISI 2/7/00

Liang Zhou, PhD
Chemistry Team Leader, HFD-180

cc: Orig. NDA 20-988
HFD-180/Division File
HFD-180/LTalarico
HFD-180/CSO/MWalsh
HFD-820/JGibbs
HFD-180/LZhou
HFD-180/MKowblansky
c:\wordfiles\chem\N20988002.4MK

Redacted 3

pages of trade

secret and/or

confidential

commercial

information

Chem. manufacturing and controls

AUG 18 2000

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

NDA: 20-988 Chem. Review: #5 Review Date: 8/14/00

Submission Type	Document Date	CDER Date	Assigned Date
BC	May 5, 2000	May 5, 2000	May 12, 2000
BZ	May 2, 2000	May 2, 2000	May 10, 2000
BC	January 19, 2000	January 20, 2000	
AC	August 31, 1999	September 1, 1999	
Original	July 20, 1998, 1998	July 22, 1998	

Name and Address of Applicant:

Wyeth Ayerst Laboratories
P.O. Box 8299
Philadelphia, PA 19101-8299

Drug Product Name:

Proprietary:	PROTONIX™
Non-proprietary/USAN and CAS:	pantoprazole sodium
Code Number (CAS):	164579-32-2
Code Number (laboratory):	B8610-23, B8610-023 (Byk-Gulden)
	WAY-140951 (Wyeth-Ayerst code)
Chem. Type/Ther. Class	Type IS

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

Pharmacological Category /Indications:

- proton pump inhibitor
- short term gastric acid suppression in GERD patients unable to take oral medication

Dosage Form: lyophilized powder for reconstitution

Strength: 40 mg (pantoprazole) per vial

Route of Administration: intravenous

How Dispensed: Rx OTC

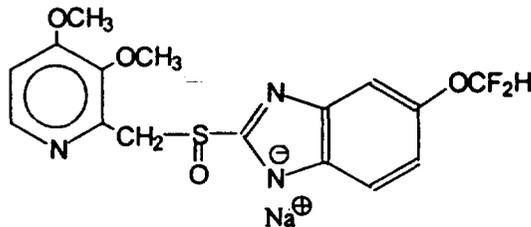
Special Product: No Yes

Chemical Name, Molecular Formula, Molecular Weight, Structural Formula

Chemical Name:

Sodium-[5-(difluoromethoxy)-2-[(3,4-dimethoxy-2-pyridyl)-methyl]-sulfinyl]-1H-benzimidazole sesquihydrate

Structure:



Molecular Formula: C₁₆H₁₄F₂N₃NaO₄S x 1.5 H₂O

Molecular Weight: 432.4 (includes water)

Related Documents: NDA 20-987

Supporting Documents

DMF	SUBJECT	DMF HOLDER	STATUS	REVIEW DATE	LETTER DATE
	Drug Substance Manufacturer	Byk Gulden	Adequate	1/14/00	2/4/99 4/5/99 11/23/99
	Rubber closure supplier		Adequate	5/13/99	-----
	Glass vial supplier		Not reviewed*	-----	-----
	Glass vial supplier		Not reviewed*	-----	-----

*It is not our practice to review DMFs for USP glass containers.

Consults:

Biopharm. Review. Approval is recommended. See report from David Udo, Ph.D.

Sterility Review. Approval is recommended with regard to sterility assurance issues. See microbiology review from Neal Sweeny, Ph.D.

Remarks/Comments: See review

Conclusions and Recommendations: Admixtures of this product require the use of an in-line filter during administration. The experimental evidence indicates that the concentration of active in the admixture remains essentially unchanged after filtration. This application is considered Approvable, pending 1) a resolution of the chemistry issues cited in the deficiency letter at the end of this review, 2) a decision from the medical reviewer that use of an in-line filter during administration is acceptable since this product is medically necessary, and 3) completion of the Label Review.

/S/

Marie Kowblansky, PhD
Review Chemist, HFD-180

S/E/oe

/S/ 8/18/00

Liang Zhou, PhD
Chemistry Team Leader, HFD-180

- cc: Orig. NDA 20-988
- HFD-180/Division File
- HFD-180/LTalarico
- HFD-180/CSO/CPerry
- HFD-820/JGibbs
- HFD-180/LZhou
- HFD-180/MKowblansky

Redacted 6

pages of trade

secret and/or

confidential

commercial

information

Chem. Manufacturing And Controls

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

SEP 14 2000

NDA: 20-988 Chem. Review: #6 Review Date: 9/14/00

Submission Type	Document Date	CDER Date	Assigned Date
BC	August 30, 2000	August 31, 2000	September 6, 2000
BC	May 5, 2000	May 5, 2000	May 12, 2000
BZ	May 2, 2000	May 2, 2000	May 10, 2000
BC	January 19, 2000	January 20, 2000	
AC	August 31, 1999	September 1, 1999	
Original	July 20, 1998, 1998	July 22, 1998	

Name and Address of Applicant:

Wyeth Ayerst Laboratories
P.O. Box 8299
Philadelphia, PA 19101-8299

Drug Product Name:

Proprietary:	PROTONIX™
Non-proprietary/USAN and CAS:	pantoprazole sodium
Code Number (CAS):	164579-32-2
Code Number (laboratory):	B8610-23, B8610-023 (Byk-Gulden)
	WAY-140951 (Wyeth-Ayerst code)
Chem. Type/Ther. Class	Type IS

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

Pharmacological Category /Indications:

- proton pump inhibitor
- short term gastric acid suppression in GERD patients unable to take oral medication

Dosage Form: lyophilized powder for reconstitution

Strength: 40 mg (pantoprazole) per vial

Route of Administration: intravenous

How Dispensed: Rx OTC

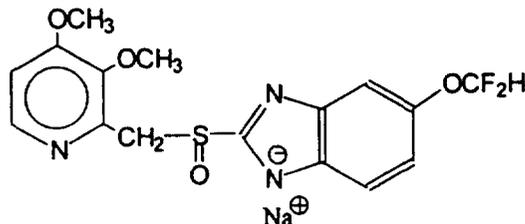
Special Product: No Yes

Chemical Name, Molecular Formula, Molecular Weight, Structural Formula

Chemical Name:

Sodium-[5-(difluoromethoxy)-2-[(3,4-dimethoxy-2-pyridyl)-methyl]-sulfinyl]-1H-benzimidazole sesquihydrate

Structure:



Molecular Formula: C₁₆H₁₄F₂N₃NaO₄S x1.5 H₂O

Molecular Weight: 432.4 (includes water)

Related Documents: NDA 20-987

Supporting Documents

DMF	SUBJECT	DMF HOLDER	STATUS	REVIEW DATE	LETTER DATE
	Drug Substance Manufacturer	Byk Gulden	Adequate	1/14/00	2/4/99 4/5/99 11/23/99
	Rubber closure supplier		Adequate	5/13/99	-----
	Glass vial supplier		Not reviewed*	-----	-----
	Glass vial supplier		Not reviewed*	-----	-----

*It is not our practice to review DMFs for USP glass containers.

Consults:

Biopharm. Review. Approval is recommended. See report from David Udo, Ph.D.

Sterility Review. Approval is recommended with regard to sterility assurance issues. See microbiology review from Neal Sweeny, Ph.D.

Remarks/Comments: See review

Conclusions and Recommendations: Admixtures of this product require the use of an in-line filter during administration. The experimental evidence indicates that the concentration of active in the admixture remains essentially unchanged after filtration. This application is considered Approvable, pending 1) revision of the proposed specification, 2) a decision from the medical reviewer that due to the medical necessity for this product use of an in-line filter during administration is acceptable, and 3) completion of the Label Review.

ISI
 Marie Kowblansky, PhD
 Review Chemist, HFD-180

9/14/00

ISI
 Liang Zhou, PhD
 Chemistry Team Leader, HFD-180

cc: Orig. NDA 20-988
 HFD-180/Division File
 HFD-180/LTalarico
 HFD-180/CSO/CPerry
 HFD-820/JGibbs
 HFD-180/LZhou
 HFD-180/MKowblansky

Redacted 2

pages of trade

secret and/or

confidential

commercial

information

Chem. manufacturing And Controls

NOV 21 2000

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

NDA: 20-988

Chem. Review: #7

Review Date: 11/20/00

Submission Type	Document Date	CDER Date	Assigned Date
BC	November 3, 2000	November 6, 2000	November 8, 2000
BC	August 30, 2000	August 31, 2000	September 6, 2000
BC	May 5, 2000	May 5, 2000	May 12, 2000
BZ	May 2, 2000	May 2, 2000	May 10, 2000
BC	January 19, 2000	January 20, 2000	
AC	August 31, 1999	September 1, 1999	
Original	July 20, 1998, 1998	July 22, 1998	

Name and Address of Applicant:

Wyeth Ayerst Laboratories
 P.O. Box 8299
 Philadelphia, PA 19101-8299

Drug Product Name:

Proprietary:	PROTONIX™
Non-proprietary/USAN and CAS:	pantoprazole sodium
Code Number (CAS):	164579-32-2
Code Number (laboratory):	B8610-23, B8610-023 (Byk-Gulden) WAY-140951 (Wyeth-Ayerst code)
Chem. Type/Ther. Class	Type IS

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

Pharmacological Category /Indications:

- proton pump inhibitor
- short term gastric acid suppression in GERD patients unable to take oral medication

Dosage Form: lyophilized powder for reconstitution

Strength: 40 mg (pantoprazole) per vial

Route of Administration: intravenous

How Dispensed: Rx OTC

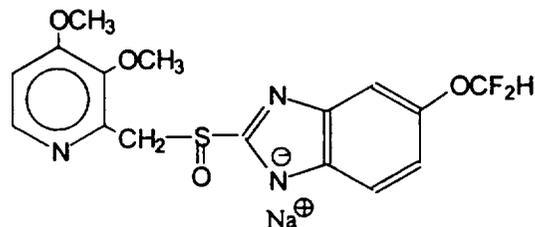
Special Product: No Yes

Chemical Name, Molecular Formula, Molecular Weight, Structural Formula

Chemical Name:

Sodium-[5-(difluoromethoxy)-2-[[[(3,4-dimethoxy-2-pyridyl)-methyl]-sulfinyl]-1H-benzimidazole sesquihydrate

Structure:



Molecular Formula: C₁₆H₁₄ F₂N₃NaO₄S x1.5 H₂O

Molecular Weight: 432.4 (includes water)

Related Documents: NDA 20-987

Supporting Documents

DMF	SUBJECT	DMF HOLDER	STATUS	REVIEW DATE	LETTER DATE
	Drug Substance Manufacturer	Byk Gulden	Adequate	1/14/00	2/4/99 4/5/99 11/23/99
	Rubber closure supplier		Adequate	5/13/99	---
	Glass vial supplier		Not reviewed*	---	---
	Glass vial supplier		Not reviewed*	---	---

*It is not our practice to review DMFs for USP glass containers.

Consults:

Biopharm. Review. Approval is recommended. See report from David Udo, Ph.D.

Sterility Review. Approval is recommended with regard to sterility assurance issues. See microbiology review from Neal Sweeny, Ph.D.

Remarks/Comments: See review

Conclusions and Recommendations: Admixtures of this product require the use of an in-line filter during administration. The experimental evidence indicates that the concentration of active in the admixture remains essentially unchanged after filtration. This application is considered Approvable, pending 1) a decision from the medical reviewer that due to the medical necessity for this product use of an in-line filter during administration is acceptable and 2) completion of the Label Review when the applicant revises the labeling to reflect the co-packaging of a filter with the product.

JS
Marie Kowblansky, PhD
Review Chemist, HFD-180

11/20/00

JS
Liang Zhou, PhD
Chemistry Team Leader, HFD-180

cc: Orig. NDA 20-988
HFD-180/Division File
HFD-180/LTalarico
HFD-180/CPerry
HFD-820/JGibbs
HFD-180/LZhou
HFD-180/MKowblansky

Redacted 2

pages of trade

secret and/or

confidential

commercial

information

Chem. manufacturing And Controls

MAR - 6 2001

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

NDA: 20-988

Chem. Review: #8

Review Date: 2/26/01

Submission Type	Document Date	CDER Date	Assigned Date
BL	February 22, 2001	February 23, 2001	February 26, 2001
BL	February 21, 2001	February 22, 2001	February 26, 2001
AZ	January 19, 2001	January 22, 2001	February 26, 2001
BC	November 3, 2000	November 6, 2000	November 8, 2000
BC	August 30, 2000	August 31, 2000	September 6, 2000
BC	May 5, 2000	May 5, 2000	May 12, 2000
BZ	May 2, 2000	May 2, 2000	May 10, 2000
BC	January 19, 2000	January 20, 2000	
AC	August 31, 1999	September 1, 1999	
Original	July 20, 1998, 1998	July 22, 1998	

Name and Address of Applicant:

Wyeth Ayerst Laboratories
P.O. Box 8299
Philadelphia, PA 19101-8299

Drug Product Name:

Proprietary:	PROTONIX™
Non-proprietary/USAN and CAS:	pantoprazole sodium
Code Number (CAS):	164579-32-2
Code Number (laboratory):	B8610-23, B8610-023 (Byk-Gulden) WAY-140951 (Wyeth-Ayerst code)
Chem. Type/Ther. Class	Type 3S

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

Pharmacological Category /Indications:

- proton pump inhibitor
- short term gastric acid suppression in GERD patients unable to take oral medication

Dosage Form: lyophilized powder for reconstitution

Strength: 40 mg (pantoprazole) per vial

Route of Administration: intravenous

How Dispensed: Rx OTC

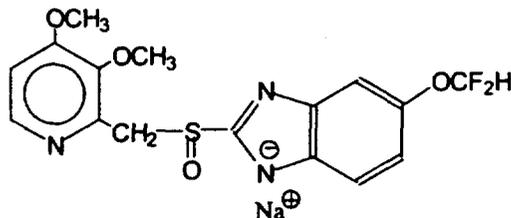
Special Product: No Yes

Chemical Name, Molecular Formula, Molecular Weight , Structural Formula

Chemical Name :

Sodium-[5-(difluoromethoxy)-2-[[[(3,4-dimethoxy-2-pyridyl)-methyl]-sulfinyl]-1H-benzimidazole sesquihydrate

Structure:



Molecular Formula: C₁₆H₁₄F₂N₃NaO₄S x1.5 H₂O
Molecular Weight: 432.4 (includes water)

Related Documents: NDA 20-987

Supporting Documents

DMF	SUBJECT	DMF HOLDER	STATUS	REVIEW DATE	LETTER DATE
	Drug Substance Manufacturer	Byk Gulden	Adequate	1/14/00	2/4/99 4/5/99 11/23/99
	Rubber closure supplier		Adequate	5/13/99	---
	Glass vial supplier		Not reviewed*	---	---
	Glass vial supplier		Not reviewed*	---	---

*It is not our practice to review DMFs for USP glass containers.

Consults:

Biopharm. Review. Approval is recommended. See report from David Udo, Ph.D.

Sterility Review. Approval is recommended with regard to sterility assurance issues. See microbiology review from Neal Sweeny, Ph.D.

OPDRA: The product name was judged to be acceptable

Compliance: All establishments were found acceptable in 1999. The Office of Compliance has notified us that as of 3/1/01 are still considered acceptable.

Remarks/Comments: From the CMC review of this application it was determined that admixtures of this product require the use of an in-line filter (≤ 5.0 micron) during administration. On consideration of this conclusion, a decision was made by ORM to require co-packaging of a filter with the product. (This was communicated to the sponsor in correspondence dated November 2, 2000.) The current submission deals with issues related to the co-packaging and labeling; all other CMC issues were resolved earlier.

Conclusions and Recommendations: This application is considered Approvable, pending 1) resolution of the co-packaging issues cited in the Draft Deficiency Letter and 2) completion of the Label Review.

Marie Kowblansky, PhD
 Review Chemist, HFD-180

Liang Zhou, PhD
 Chemistry Team Leader, HFD-180

cc: Orig. NDA 20-988
 HFD-180/Division File
 HFD-180/LTalarico
 HFD-180/CPerry
 HFD-820/CHoiberg
 HFD-180/LZhou
 HFD-180/MKowblansky

/s/

Marie Kowblansky
3/6/01 05:19:55 PM
CHEMIST

Liang Zhou
3/6/01 05:42:20 PM
CHEMIST

Please refer to the proposed Phase IV commitments pending final resolution with CMC IR issued last week . Telecon min. dated 9/21 and 9/29/00 also supports our conclusion .

Redacted 3

pages of trade

secret and/or

confidential

commercial

information

Chem. manufacturing And Controls

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

NDA: 20-988 Chem. Review: #9 Review Date: 3/6/01

Submission Type	Document Date	CDER Date	Assigned Date
BC	March 6, 2001	March 6, 2001 (FAX)	March 6, 2001
BL	February 22, 2001	February 23, 2001	February 26, 2001
BL	February 21, 2001	February 22, 2001	February 26, 2001
AZ	January 19, 2001	January 22, 2001	February 26, 2001
BC	November 3, 2000	November 6, 2000	November 8, 2000
BC	August 30, 2000	August 31, 2000	September 6, 2000
BC	May 5, 2000	May 5, 2000	May 12, 2000
BZ	May 2, 2000	May 2, 2000	May 10, 2000
BC	January 19, 2000	January 20, 2000	
AC	August 31, 1999	September 1, 1999	
Original	July 20, 1998, 1998	July 22, 1998	

Name and Address of Applicant:

Wyeth Ayerst Laboratories
P.O. Box 8299
Philadelphia, PA 19101-8299

Drug Product Name:

Proprietary:	PROTONIX™
Non-proprietary/USAN and CAS:	pantoprazole sodium
Code Number (CAS):	164579-32-2
Code Number (laboratory):	B8610-23, B8610-023 (Byk-Gulden) WAY-140951 (Wyeth-Ayerst code)
Chem. Type/Ther. Class	Type 3S

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

Pharmacological Category /Indications:

- proton pump inhibitor
- short term gastric acid suppression in GERD patients unable to take oral medication

Dosage Form: lyophilized powder for reconstitution

Strength: 40 mg (pantoprazole) per vial

Route of Administration: intravenous

How Dispensed: Rx OTC

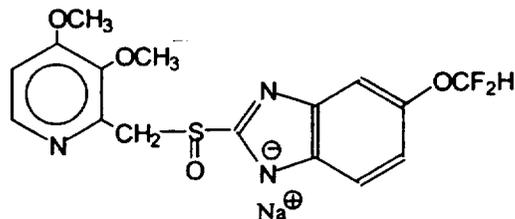
Special Product: No Yes

Chemical Name, Molecular Formula, Molecular Weight, Structural Formula

Chemical Name:

Sodium-[5-(difluoromethoxy)-2-[(3,4-dimethoxy-2-pyridyl)-methyl]-sulfinyl]-1H-benzimidazole sesquihydrate

Structure:



Molecular Formula: C₁₆H₁₄ F₂N₃NaO₄S x1.5 H₂O

Molecular Weight: 432.4 (includes water)

Related Documents: NDA 20-987

Supporting Documents

DMF	SUBJECT	DMF HOLDER	STATUS	REVIEW DATE	LETTER DATE
	Drug Substance Manufacturer	Byk Gulden	Adequate	1/14/00	2/4/99 4/5/99 11/23/99
	Rubber closure supplier		Adequate	5/13/99	----
	Glass vial supplier		Not reviewed*	----	----
	Glass vial supplier		Not reviewed*	----	----

*It is not our practice to review DMFs for USP glass containers.

Consults:

Biopharm. Review. Approval is recommended. See report from David Udo, Ph.D.

Sterility Review: Approval is recommended with regard to sterility assurance issues. See microbiology review from Neal Sweeny, Ph.D.

OPDRA: The product name was judged to be acceptable

Compliance: All establishments were found acceptable in 1999. The Office of Compliance has notified us that as of 3/1/01 they are still considered acceptable.

Remarks/Comments:

Conclusions and Recommendations: From a CMC perspective this application can be approved with 24 month expiration. The applicant should provide a commitment to conduct the requested Phase IV studies.

Marie Kowblansky, PhD
Review Chemist, HFD-180

Liang Zhou, PhD
Chemistry Team Leader, HFD-180

cc: Orig. NDA 20-988
HFD-180/Division File
HFD-180/LTalarico
HFD-180/CPerry
HFD-820/CHOiberg
HFD-180/LZhou
HFD-180/MKowblansky

/s/

Marie Kowblansky
(3/9/01 01:15:20 PM
CHEMIST

Liang Zhou
3/12/01 02:35:11 PM
CHEMIST

I concurred the review chemist's Approval recommendation with the Phase IV Commitments [please refer to CMC Review #8 and Phase IV stability studies for the filter in this submission [BL] dated on 2/23/01].

Redacted 3

pages of trade

secret and/or

confidential

commercial

information

Chem. manufacturing And Controls