AGRANULOCYTOSIS	1
LEUCOPENIA	5

Adverse reactions to drugs Date: 1999-05-27

Search covers total holding

Summary on investigated terms

PANTOPRAZOLE

ALOPECIA	2
ANAEMIA HAEMOLYTIC	1
ANOREXIA	2
ARTHRALGIA	1
BLINDNESS	1
CHEST PAIN	1
COLD URTICARIA	1
COMA	1
CONFUSION	1
CONVULSIONS GRAND MAL	1
DEAFNESS	1
DIARRHOEA	3
DIZZINESS	1
ENCEPHALOPATHY	1
EPIDERMAL NECROLYSIS	1
FIXED ERUPTION	1
HEADACHE	1
HEPATIC ENZYMES INCREASED	2
HEPATITIS	2
HYPERKALAEMIA	1
IMPOTENCE	1
JAUNDICE	1
LARYNX OEDEMA	1
LEUCOPENIA	1
LIBIDO DECREASED	1
MALAISE	1
MYALGIA	1
NEPHRITIS INTERSTITIAL	1
NERVOUSNESS	2
NEUROPATHY	2
NPN INCREASED	1
OEDEMA	1
OEDEMA PERIPHERAL	1
PARAESTHESIA	2
PARESIS	1
PERIPHERAL ISCHAEMIA	1
PRURITUS	7
RASH	2
RASH ERYTHEMATOUS	2
RASH MACULO-PAPULAR	3
SEBORRHOEA	1
SUDDEN DEATH	1
TONGUE OEDEMA	1
VOMITING	2
WEIGHT DECREASE	1

PANTOPRAZOLE SODIUM

ABDOMINAL PAIN	17
ABORTION	2

Adverse reactions to drugs Date: 1999-05-27

Search covers total holding

Summary on investigated terms

ACNE	1
AGGRESSIVE REACTION	1
AGITATION	2
AGRANULOCYTOSIS	1
ALLERGIC REACTION	3
ALOPECIA	4
AMNESIA	2
ANAEMIA HAEMOLYTIC	1
ANAESTHESIA MOUTH	1
ANAL FISSURE	1
ANAPHYLACTIC SHOCK	3
ANAPHYLACTOID REACTION	1
ANGINA PECTORIS	1
ANGINA PECTORIS AGGRAVATED	1
ANGIOEDEMA	7
ANXIETY	4
APPETITE INCREASED	1
ARRHYTHMIA	3
ARTHRALGIA	5
ARTHROPATHY	1
ARTHROSIS	1
ASPIRATION	1
ASTHENIA	2
ASTHMA	2
ATAXIA	3
BACK PAIN	2
BILIRUBINAEMIA	1
BLADDER CARCINOMA	1
BLINDNESS TEMPORARY	1
BREAST ENLARGEMENT	4
BRONCHOSPASM	3
BRONCHOSPASM AGGRAVATED	1
BULLOUS ERUPTION	3
BUNDLE BRANCH BLOCK	1
CARDIAC FAILURE	1
CARDIAC FAILURE LEFT	1
CEREBELLAR SYNDROME	1
CEREBROVASCULAR DISORDER	4
CHEST PAIN	6
CIRCULATORY FAILURE	3
COAGULATION TIME DECREASED	1
COAGULATION TIME INCREASED	3
COMA	2
CONDITION AGGRAVATED	1
CONFUSION	4
CONSTIPATION	3
CONVULSIONS	1

CONVULSIONS GRAND MAL	2
COUGHING	1
CRAMPS LEGS	1
CREATINE PHOSPHOKINASE INC	1
CYSTITIS	2
DEPRESSION	17

Adverse reactions to drugs Date: 1999-05-27

Search covers total holding

Summary on investigated terms

DERMATITIS	1
DERMATITIS EXFOLIATIVE	1
DIARRHOEA	31
DIARRHOEA BLOODY	1
DIPLOPIA	2
DIZZINESS	30
DREAMING ABNORMAL	2
DYSAESTHESIA	6
DYSPEPSIA	4
DYSPHAGIA	3
DYSPNOEA	8
DYSURIA	1
ECZEMA	3
EMBOLISM PULMONARY	1
EMOTIONAL LABILITY	1
EPIDERMAL NECROLYSIS	1
EPIDIDYMITIS	1
EPISTAXIS	3
ERUCTATION	2
ERYTHEMA MULTIFORME	1
EXTRAPYRAMIDAL DISORDER	1
EXTRASYSTOLES	4
EYE ABNORMALITY	1
EYE BURNS	1
FACE OEDEMA	10
FAECES DISCOLOURED	2
FATIGUE	5
FEVER	7
FLATULENCE	8
FLUSHING	4
FURUNCULOSIS	1
GAIT ABNORMAL	1
GAMMA-GT INCREASED	3
GASTRIC ULCER	2
GASTRIC ULCER HAEMORRHAGIC	2
GASTROESOPHAGEAL REFLUX	3
GI HAEMORRHAGE	2
GINGIVITIS	1
GLAUCOMA	1
GLOSSITIS	2
GYNAECOMASTIA	3
HAEMATEMESIS	1
HAEMATURIA	1
HAEMORRHAGE NOS	1
HAEMORRHOIDS	1

HALLUCINATION	2
HEADACHE	49
HEART DISORDER	1
HEPATIC ENZYMES INCREASED	2
HEPATIC FAILURE	1
HEPATIC FUNCTION ABNORMAL	3
HEPATIC NEOPLASM	1
HEPATITIS	2

Adverse reactions to drugs Date: 1999-05-27

Search covers total holding

Summary on investigated terms

HEPATITIS CHOLESTATIC	1
HEPATOCELLULAR DAMAGE	1
HEPATORENAL SYNDROME	1
HERNIA CONGENITAL	1
HYPERAESTHESIA	1
HYPERKINESIA	1
HYPERPYREXIA	1
HYPERTENSION	2
HYPERTONIA	1
HYPOAESTHESIA	1
HYPOTENSION	2
HYPOTENSION POSTURAL	2
HYSTERIA	1
IMPOTENCE	3
INFECTION	1
INFECTION VIRAL	1
INFLUENZA-LIKE SYMPTOMS	1
INJECTION SITE INFLAMMATIO	1
INJECTION SITE PAIN	1
INJECTION SITE REACTION	1
INSOMNIA	4
JAUNDICE	3
LACRIMATION ABNORMAL	1
LARYNGISMUS	1
LEUCOPENIA	6
LEUKAEMIA GRANULOCYTIC	1
LEUKORRHOEA	1
LYMPHOMA MALIGNANT	1
MALAISE	14
MICTURITION FREQUENCY	3
MIGRAINE	4
MONILIASIS	2
MOUTH DRY	3
MUSCLE CONTRACTIONS INVOLU	1
MUSCLE WEAKNESS	2
MYALGIA	11
MYOCARDIAL INFARCTION	4
MYOPATHY	1
NAUSEA	29
NERVOUSNESS	2
NEUROPATHY	2
NIPPLE ULCERATION	1
NPN INCREASED	1

OEDEMA	6
OEDEMA GENERALISED	1
OEDEMA PERIORBITAL	3
OEDEMA PERIPHERAL	1
OESOPHAGITIS	2
OPTIC ATROPHY	1
PAIN	1
PALPITATION	5
PANCREATITIS	5
PANCYTOPENIA	3

□

Adverse reactions to drugs Date: 1999-05-27

Search covers total holding

Summary on investigated terms

PARAESTHESIA	6
PARALYSIS	2
PARESIS	1
PARKINSONISM AGGRAVATED	1
PARONIRIA	2
PAROSMIA	2
PEPTIC ULCER HAEMORRHAGIC	1
PHLEBITIS	1
PHOTOSENSITIVITY REACTION	4
PLEURAL MESOTHELIOMA	1
PRURITUS	28
PSORIASIS AGGRAVATED	2
PSYCHOSIS	2
PURPURA	1
RASH	28
RASH ERYTHEMATOUS	15
RASH MACULO-PAPULAR	10
RASH PUSTULAR	1
RENAL FAILURE ACUTE	1
RENAL FUNCTION ABNORMAL	1
RENAL PAIN	1
RESPIRATORY DEPRESSION	1
RETROBULBAR NEURITIS	1
RHABDOMYOLYSIS	2
RHINITIS	2
RIGORS	4
SEXUAL FUNCTION ABNORMAL	1
SGOT INCREASED	4
SGPT INCREASED	4
SKIN COLD CLAMMY	2
SKIN DISCOLOURATION	1
SKIN DISORDER	2
SKIN DRY	2
SKIN ULCERATION	1
SLEEP DISORDER	1
SOMNOLENCE	4
SPEECH DISORDER	1
STOMATITIS ULCERATIVE	4
SUBARACHNOID HAEMORRHAGE	1
SUDDEN DEATH	1
SWEATING INCREASED	4

SYNCOPE	4
TACHYCARDIA	2
TASTE LOSS	1
TASTE PERVERSION	3
TEMPERATURE CHANGED SENSAT	2
THERAPEUTIC RESPONSE DECRE	1
THROMBOCYTHAEMIA	1
THROMBOCYTOPENIA	5
THROMBOPHLEBITIS	2
THROMBOPHLEBITIS ARM	1
THROMBOPHLEBITIS PELVIC VE	1
TINNITUS	2

Adverse reactions to drugs Date: 1999-05-27

Search covers total holding

Summary on investigated terms

TONGUE DISCOLOURATION	2
TONGUE DISORDER	1
TONGUE OEDEMA	2
TONGUE PARALYSIS	1
TRANSIENT ISCHAEMIC ATTACK	1
TREMOR	3
UNEXPECTED THERAPEUTIC EFF	1
URTICARIA	13
UTERINE HAEMORRHAGE	2
VASCULITIS	1
VASOSPASM	1
VERTIGO	3
VESICULAR RASH	1
VESTIBULAR DISORDER	2
VISION ABNORMAL	25
VISUAL FIELD DEFECT	3
VITREOUS DETACHMENT	1
VOMITING	13
WEIGHT INCREASE	2
XEROPHTHALMIA	1
	785

Search performed on:

Year(s): All

Countries: All

Drug(s): PANTOPRAZOLE
PANTOPRAZOLE SODIUM

Reaction(s): All

PEDIATRIC PAGE

(Complete for all original application and all efficacy supplements)

NDA/BLA Number:	20987	**Trade Name:**	PROTONIX (PANTOPRAZOLE SODIUM) 40MG ENTE
Supplement Number:		**Generic Name:**	PANTOPRAZOLE SODIUM
Supplement Type:		**Dosage Form:**	DRT
Regulatory Action:	AP	**Proposed Indication:**	Short-term treatment of erosive esophagitis associated with gastroesophageal reflux disease (GERD)

ARE THERE PEDIATRIC STUDIES IN THIS SUBMISSION?

NO. No waiver and no pediatric data

What are the INTENDED Pediatric Age Groups for this submission?

____NeoNates (0-30 Days) ____Children (25 Months-12 years)

____Infants (1-24 Months) ____Adolescents (13-16 Years)

Label Adequacy Does Not Apply

Formulation Status

Studies Needed

Study Status

Are there any Pediatric Phase 4 Commitments in the Action Letter for the Original Submission? NO

COMMENTS:

In the approval letter, we will defer pediatric studies. The sponsor submitted a PPSR on 6/7/99 and was issued an inadequacy letter on 11/9/99.

The sponsor submitted a PPSR to IND —— on 6/7/99. An inadequacy letter was issued on 11/9/99.

This Page was completed based on information from a PROJECT MANAGER/CONSUMER SAFETY OFFICER.

MARIA WALSH

Signature /S/ _____ Date 1/24/00

APPEARS THIS WAY
ON ORIGINAL

PEDIATRIC PAGE

(Complete for all original application and all efficacy supplements)

NDA/BLA Number:	20987	**Trade Name:**	PROTONIX (PANTOPRAZOLE SODIUM) 40MG ENTE
Supplement Number:		**Generic Name:**	PANTOPRAZOLE SODIUM
Supplement Type:		**Dosage Form:**	DRT
Regulatory Action:	NA	**Proposed Indication:**	Short-term treatment of erosive esophagitis associated with gastroesophageal reflux disease (GERD)

ARE THERE PEDIATRIC STUDIES IN THIS SUBMISSION?
NO. No waiver and no pediatric data

What are the INTENDED Pediatric Age Groups for this submission?

____NeoNates (0-30 Days.)____Children (25 Months-12 years)
____Infants (1-24 Months) ____Adolescents (13-16 Years)

Label Adequacy	Does Not Apply
Formulation Status	-
Studies Needed	-
Study Status	-

Are there any **Pediatric Phase 4 Commitments in the Action Letter for the Original Submission?** NO

COMMENTS:
In the approval letter, we will defer pediatric studies and request the sponsor to submit a pediatric drug development plan and a proposed pediatric study request.

This Page was completed based on information from a PROJECT MANAGER/CONSUMER SAFETY OFFICER, MARIA WALSH

/S/ _____ 5/10/99

Signature Date

APPEARS THIS WAY
ON ORIGINAL

Barry Winston, M.D.
Houston Medical Research Associates
800 Peakwood Dr.
Suite 5D
Houston, Texas 77090

MAY 12 1999

Dear Dr. Winston,

Between 13 and 19 January 1999, Ms. A. Branche, from the Food and Drug Administration (FDA), inspected your conduct of a clinical study of the investigational drug Protonix Tablets (pantoprazole). You conduct this study for Wyeth-Ayerst Research. This inspection is a part of FDA's Bioresearch Monitoring Program, which includes inspections designed to validate studies on which drug approval may be based and to assure that the rights and welfare of the human subjects of those studies have been protected.

From our evaluation of the inspection report and the documents collected during the inspection, we conclude that you did not adhere to the Federal regulations and/or good clinical practices that govern your conduct of clinical studies and the protection of human subjects in the following aspects: the drug accountability records inaccurately report that subject #037 returned study drug on 4 September 1997. This subject missed the third study visit on 4 September 1997.

Please make appropriate corrections/changes in your procedures to assure that the finding noted above is not repeated in any of your ongoing or future studies.

We appreciate the cooperation shown Ms. Branche during the inspection.

Sincerely yours,

Bette Barton, Ph.D, M.D.
Chief
Good Clinical Practice Branch I
Division of Scientific Investigations
Office of Medical Policy
Center for Drug Evaluation and Research.
7520 Standish Place
Rockville, Maryland 20855

OFFICE	SURNAME	DATE	OFFICE	SURNAME	DATE
344 -1	/ST	5/12/99	-	-	

FILE
CC:

cc:
HFA-224
HFD-180 Doc. Rm. NDA .# 20987
HFD-180 Review Div. Dir. Talarico, L.
HFD-180 MO Gallo-Torres
HFD-180 PM Walsh
HFD-340/Reading File
HFD-344/ Chron File
HFD-344/ CIB File # 9719.
HFD-344/ CIB Reviewer Malek
HFD-344/ Currier
HFR-SW150 DIB Deininger
HFR-SW1540 BIMO MONITOR Martinez
HFR-SW1580 FIELD INVESTIGATOR Branche

CFN: 1650748
Field Classification: NAI
Headquarters Classification:
_____1)NAI
__X__2)VAI-no response required
_____3)VAI-response requested
_____4)OAI

If the Field and Headquarters classifications are different, explain why:

Deficiencies noted:
----------inadequate consent form
----------inadequate drug accountability
----------deviations from protocol
----------inadequate records
----------failure to report ADRs
-----x-------other (specify): inaccurate records

Note to M.O.
1. Thirty subjects were enrolled and all completed the study.
2. Records of 9 subjects were reviewed.
3. All ADRs were reported.
4. Data appears acceptable to support the drug claims.

APPEARS THIS WAY
ON ORIGINAL

r/d:KM:3/29/99
corrected:BLB:3/30/99
corrected:slk:5/6/99
finaled:slk:5/11/99

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

MAR 25 1999

Thomas Kovacs, M.D.
11301 Wilshire Blvd, Bldg. 115, Rm 212
Los Angeles, CA 90073

Dear Dr. Kovacs,

Between 22 January 1999 and 1 February 1999, Mr. Roland L. Koller from the Food and Drug Administration (FDA) conducted an inspection of your conduct as the investigator for the clinical study (protocol #3001 A1-301 - US) of the investigational drug Protonix (pantoprazole sodium tablets). You conducted this study for Wyeth-Ayerst Research. This inspection is a part of FDA's Bioresearch Monitoring Program, which includes inspections designed to validate studies on which drug approval may be based and to assure that the rights and welfare of the human subjects of those studies have been protected.

From our evaluation of the inspection report and the documents collected during the inspection, we conclude that you did not adhere to all the pertinent Federal regulations and/or good clinical practices governing your conduct of clinical investigations and the protection of human subjects in the following respects:

1. Investigators are required to conduct studies in accordance with the protocol [21 CFR 312.53 (c) (1) (vi) (a)].

In violation of the protocol you enrolled subject #031 in the study within a month of the subject's using omeprazole [protocol section 7.2].

2. Investigators are required to maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual administered the investigational drug [21 CFR 312.62(b)].

The CRF for subject # 001 failed to report the mild symptoms of acid regurgitation that were reported in this subject's diary for 27 May 1997.

Please make appropriate corrections/changes in your procedures to assure that the findings noted above are not repeated in any of your ongoing or future studies.

We appreciate the cooperation shown Mr. Koller during the inspection.

Sincerely yours,

/S/

Bette Barton, Ph.D, M.D.
Chief
Clinical Investigation Branch I
Good Clinical Practices Branch
Division of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research.

cc:
HFA-224
HFD-180 Doc. Rm. NDA .# 20987
HFD-180 Review Div. Dir. Talarico, L.
HFD-180 MO Gallo-Torres
HFD-180 PM Walsh
HFD-340/Reading File
HFD-344/ Chron File
HFD-344/ CIB File # 9263.
HFD-344/ CIB Reviewer Malek
HFD-344/ Currier
HFR-PA250 DIB Kozick
HFR-PA2565 BIMO MONITOR Koller
HFR-PA2585 FIELD INVESTIGATOR Koller

CFN: 2060793
Field Classification: NAI
Headquarters Classification:
_____1)NAI
_ X _ 2)VAI-no response required
_____3)VAI-response requested
_____4)OAI

If the Field and Headquarters classifications are different, explain why:

Deficiencies noted:
__ __ inadequate consent form
__ __ inadequate drug accountability
__X__ deviations from protocol
__X _ inadequate records
_____ failure to report ADRs
_____ other (specify)

r/d: KM:2/24/99
reviewed:BLB:3/22/99
finaled:slk:3/22/99

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

MAR 1 1 1999

Rao Movva, M.D..
545 Valley View Dr.
Moline, IL 61265

Dear Dr. Movva

On January 12-15, 1999, Ms. Susan Yuscius and Mr. Thomas Nojek representing the Food and Drug Administration (FDA), conducted an inspection of your conduct, as the investigator of record of a clinical study of the investigational drug Protonix (pantoprazole sodium) tablets, performed for Wyeth-Ayerst Research. . This inspection is a part of FDA's Bioresearch Monitoring Program, which includes inspections designed to validate studies on which drug approval may be based and to assure that the rights and welfare of the human subjects of those studies have been protected.

From an evaluation of the inspection report and of the documents collected during the inspection we conclude that there were no substantial departures from pertinent federal regulations and/or good clinical investigational practices governing your conduct of clinical investigations and the protection of human subjects.

We appreciate the cooperation shown our personnel during the inspection.

Sincerely yours,

/S/

Bette Barton, Ph.D, M.D.
Chief
Clinical Investigation Branch I
Good Clinical Practices
Division of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research.

APPEARS THIS WAY
ON ORIGINAL

cc:
HFA-224
HFD-180 Doc. Rm. NDA .# 20987.
HFD-180 Review Div. Dir. Talarico, L.
HFD-180 MO Gallo-Torres
HFD-180 PM Walsh
HFD-340/Reading File
HFD-344/ Chron File
HFD-344/ CIB File # 9701
HFD-344/ CIB Reviewer Malek
HFD-344/ Currier
HFR-CE650 DIB Baumgarten
HFR-CE6520 BIMO MONITOR Yuscius
HFR-CE6520 FIELD INVESTIGATOR Nojek

CFN: 1424272
Field Classification: NAI
Headquarters Classification:
__X_1)NAI
_ _ 2)VAI-no response required
_____3)VAI-response requested
_____4)OAI
r/d:KM:2/23/99
review:AEH:3/9/99
finaled:slk:3/10/99

Note to M.O.

1. This site was chosen because of the relatively larger number of subjects.
2. 32 subjects were enrolled, 6 did not fit the inclusion/exclusion criteria and 26 completed the study.
3. 12 subjects reached the end point at 4 weeks, and 14 completed 8 weeks.
4. There were no ADRs reported.
5. The data appears acceptable to support the drug claim.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20-987

CORRESPONDENCE

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: November 23, 1999

FROM: Maria R. Walsh. Regulatory Project Manager. HFD-180 /S/ 11/23/99

SUBJECT: NDA 20-987; Protonix (pantoprazole sodium) Delayed-Release Tablets; Labeling Revisions

TO: NDA 20-987

BACKGROUND: NDA 20-987. Protonix (pantoprazole sodium) Delayed-Release Tablets was approvable on June 30, 1999 for the short-term treatment of erosive esophagitis. Wyeth-Ayerst responded to the approvable letter in a July 30, 1999 Class 2 resubmission containing proposed revised draft labeling (as well as chemistry and biopharmaceutics information).

The revised draft labeling was reviewed by the Division and further revisions were made based on the following reviews: Medical Team Leader review (dated 9/17/99), Pharmacology Team Leader review (dated 11/4/99). Chemistry review (dated 11/3/99), and Biopharmaceutics review (dated 11/3/99) (see attached labeling dated 11/14/99).

The FDA's revised draft labeling (dated 11/14/99) was discussed at a team meeting on November 17, 1999 and the following changes were made.

1. **CLINICAL PHARMACOLOGY, Pharmacokinetics:**

The second paragraph regarding ———————— was deleted. Since serum pantoprazole accumulation is not considered clinically significant, inclusion of this information was not considered useful. It was noted that information regarding pantoprazole metabolism is included under the ***Metabolism*** subsection.

2. **CLINICAL PHARMACOLOGY, Pharmacodynamics, *Enterochromaffin-Like (ECL) Cell Effects:***

Per a discussion regarding where and how to convey the carcinogenicity and genotoxicity findings with this drug, the following (last) sentence in the second paragraph was deleted:

[ ]

However, following a post-meeting discussion, the Office Director decided to replace the above sentence with the following sentence:

[redacted] (see **PRECAUTIONS, Carcinogenesis, Mutagenesis, Impairment of Fertility**)."

3. **INDICATIONS AND USAGE:**

Per a discussion regarding how to convey that the drug should not be used for maintenance therapy in light of the carcinogenicity and genotoxicity findings, the following was deleted from the end of the first paragraph:

[redacted]

The sponsor's sentence was retained (as the second paragraph) as follows:

"The safety and efficacy of PROTONIX for maintenance therapy (e.g., beyond 16 weeks) have not been established (see **PRECAUTIONS).**"

4. **PRECAUTIONS, General:**

The first paragraph regarding dosing and hepatic impairment was moved down to become the third paragraph.

Per a discussion regarding what should be conveyed in this section about the genotoxicity findings with this drug in light of the labeling for [redacted], Delayed-Release Tablets, which includes 4 positive genotoxicity assays but does not include a statement in the **PRECAUTIONS** section, the second paragraph was revised as follows:

"The safety and efficacy of PROTONIX for maintenance therapy (e.g., beyond 16 weeks) have not been established. Pantoprazole is carcinogenic in rodents and caused rare types of gastrointestinal tumors. While the relevance of these animal findings to human risk is unknown, PROTONIX should not be used as maintenance therapy (see **INDICATIONS AND USAGE**)."

After the meeting, the Office Director decided to replace "should not be used as maintenance therapy" with "is not indicated for maintenance therapy."

cc:
Orig NDA 20-987
HFD-180/Div. file
HFD-180/M.Walsh
Filename: [redacted]

APPEARS THIS WAY
ON ORIGINAL

16 PAGE(S) REDACTED

Draft

Labeling

Item 8.7.4: Commercial Marketing Experience and Foreign Regulatory Actions

TABLE 1 COMMERCIAL MARKETING HISTORY OF ORAL PANTOPRAZOLE

Country	Trade Name	Company	Registration Date	Indications	Marketed (yes/no)
Argentina	Pantop Zurcal	Byk Argentina Boehringer Mannheim	17 Feb 1995	Duodenal ulcer (DU), gastric ulcer (GU), reflux esophagitis (GERD, stages 2 and3)	yes
Australia	Somac	Pharmacia & Upjohn	23 Jan 1995	DU, GU;GERD (stages 2 and 3);GI lesions refractory to H_2 blockers;Zollinger-Ellison syndrome (ZES);*H. pylori*	yes
Austria	Pantoloc Zurcal	Byk Austria Nycomed	29 June 1995 25 May 1996 (*H. pylori*)	DU, GU, GERD (stages 2 and3), *H. pylori*	yes
Bahrain	Pantozol	Al Suffar Pharma	13 May 1996	DU, GU, GERD (stages 2 and3)	yes
Belgium	Pantozol Zurcale	Byk Belga Nycomed	22 Feb 1996	DU, GU, GERD (stages 2 and3)	yes
Belize	Pantecta	Novartis	based on Guatemala registration	DU, GU, GERD	yes
Brazil	Pantozol Zurcal	Byk Quimica Boehringer Mannheim	07 Apr 1995	DU, GU, GERD (stages 2 and 3)	yes
Byelorussia	Kontrolok	Belpharm	18 Oct 1995 Feb 1997 (*H. pylori*)	DU, GU, GERD, *H. pylori*	yes
Canada[a]	Pantoloc Pantoloc Panto-Byk	Byk Canada Solvay Pharma Byk Gulden	05 July 1996	DU, GU, GERD	yes
Chile	Zurcal	Novartis	21 Nov 1996	DU, GU, GERD, H_2 antagonist refractory lesions	yes
Columbia	Zurcal	Novartis	18 Jun 1996	DU, GU, GERD	yes
Costa Rica	Pantecta	Novartis	15 Oct 1996	DU, GU, GERD	yes
Croatia	Controloc	Byk Croatia	13 Mar 1996	DU, GU, GERD (stages 2 and 3)	yes
Czech Republic	Controloc	Byk Czeska	16 Aug 1995 03 Sept 1996 (*H. pylori*)	DU, GU, GERD, *H. pylori*	yes
Denmark	Pantoloc	Nycomed	08 Aug 1995 17 June 1997 (*H. pylori*)	DU, GU, GERD, *H. pylori*	yes
Ecuador	Zurcal	Novartis	10 May 96	DU, GU, GERD, ZES H_2 antagonist refractory lesions	yes
Egypt	Controloc	EPC	08 Oct 1996	DU, GU, GERD	yes

a: Pantoloc is marketed in co-promotion by Solvay Pharma and Byk Canada. The trademark "Panto-Byk" is currently not used.

Item 8.7.4: Commercial Marketing Experience and Foreign Regulatory Actions

TABLE I COMMERCIAL MARKETING HISTORY OF ORAL PANTOPRAZOLE

Country	Trade Name	Company	Registration Date	Indications	Marketed (yes/no)
El Salvador	Pantecta	Novartis	22 Aug 1996	DU, GU, GERD, ZES H_2 antagonist refractory lesions	yes
Finland	Somac	Pharmacia & Upjohn	07 Nov 1994 09 July 1997 (*H. pylori*)	DU, GU, GERD, *H. pylori*	yes
France	Eupantol Inipomp	Byk France Synthélabo	08 Feb 1995	DU, GU, GERD	yes
Germany	Pantozol Rifun	Byk Gulden Schwarz Pharma	23 Aug 1994 05 Aug 1997 (*H. pylori*)	DU, GU, GERD (stages 2 and 3), *H. pylori*	yes
Greece	Zurcazol Pantoloc	Nycomed Synthélabo	12 Sept 1995	DU, GU, GERD	yes
Guatemala	Pantecta	Novartis	24 Apr 1996	DU, GU, GERD	yes
Honduras	Pantecta	Novartis	23 Oct 1996	DU, GU, GERD, ZES, *H. pylori*, H_2 antagonist refractory lesions	yes
Hong Kong	Pantoloc	Zuellig	15 Aug 1995	DU, GU, GERD (stages 2 and 3)	yes
Hungary	Controloc	Byk Hungary	31 Oct 1995 13 Nov 1996 (*H. pylori*)	DU, GU, GERD (stages 2 and 3), *H. pylori*	yes
Indonesia	Pantozol	Pharos	24 Dec 1996	DU, GU, GERD	yes
Ireland	Protium	Knoll	28 Sept 1995	DU, GU, GERD (stages 2 and 3)	yes
Israel	Controloc	Pharma-Clal (Bayer)	Feb 1997	DU, GU, GERD, *H. pylori*	yes
Italy	Pantorc Pantopan Peptazol Pantecta	Byk Italia Pharmacia & Upjohn Boehringer Mannheim Ravizza	02 May 1996	DU, GU, GERD (stages 2 and 3)	yes
Lebanon	Inipomp	Synthélabo	02 Apr 1997	DU, GU, GERD	yes
Luxembourg	Pantozol	Byk Belga	19 July 1995	DU, GU, GERD (stages 2 and 3)	yes
Malaysia	Controloc	Mico	21 Aug 1997	DU, GU	yes
Mexico	Pantozol Zurcal	Byk Mexico Novartis	10 June 1994 25 Nov 1994 17 June 1996 (*H. pylori*)	DU, GU, GERD, *H. pylori*, ZES, H_2 antagonist refractory lesions	yes
Morocco	Inipomp	Synthélabo	05 June 1997	DU, GU, GERD	yes
Netherlands	Pantozol Pantozol	Byk Netherlands Nycomed	06 June 1995 30 Jan 1998 (*H. pylori*)	DU, GU, GERD (stages 2 and 3), *H. pylori*	yes

b: TBD = to be decided.

Item 8.7.4: Commercial Marketing Experience and Foreign Regulatory Actions

TABLE 1 COMMERCIAL MARKETING HISTORY OF ORAL PANTOPRAZOLE

Country	Trade Name	Company	Registration Date	Indications	Marketed (yes/no)
New Zealand	Somac	Pharmacia & Upjohn	11 May 1995 01 Oct 1997 (*H. pylori*)	DU, GU, GERD, ZES, *H. pylori*	yes
Nicaragua	Pantecta	Novartis	07 Oct 1996	DU, GU, GERD, ZES, H_2 antagonist refractory lesions	yes
Norway	Somac	Pharmacia & Upjohn	04 April 1995	DU, GU, GERD	yes
Panama	Pantecta	Novartis	26 Aug 1996	DU, GU, GERD	yes
Peru	Zurcal	Novartis	24 July 1997	DU, GU, GERD, *H. pylori*, ZES, H_2 antagonist refractory lesions	yes
Philippines	Pantoloc Ulcepraz	Zuellig Pharma Ciba-Geigy	04 Dec 1996	DU, GU, GERD	yes
Poland	Controloc	Byk Roland Polska	26 Nov 1996	DU, GU, GERD, ZES, *H. pylori*	yes
Portugal	Pantoc Zurcal Apton	Byk Portugal Lab. Normal (Novartis) Lab. Delta	12 Feb 1996	DU, GU, GERD, ZES	yes
Romania	Controloc	Byk	15 May 1997	DU, GU, GERD, *H. pylori*	yes
Saudi Arabia	Pantozol	Cigala	02 July 1997	DU, GU, GERD	yes
Slovak Republic	Controloc	Byk	04 Sept 1995 15 Oct 1996 (*H. pylori*)	DU, GU, GERD, *H. pylori*	yes
Slovenia	Controloc	Byk	26 Aug 1996	DU, GU, GERD	yes
South Africa	Pantoloc Controloc	Byk-Madaus Bayer	24 Feb 1994 13 Aug 1994 19 Jan 1996 (*H. pylori*)	DU, GU, GERD, *H. pylori*	yes
Spain	Pantecta Pantecta Anagastra Ulcotenal	Byk Elmu Pharmacia & Upjohn Madaus Cerafarm Recordati	05 March 1996 31 Jan 1996 19 Dec 1995 Feb 1998 (*H. pylori*)	DU, GU, GERD (stages 2 and 3), *H. pylori*	yes
Sweden	Pantoloc Pantoloc	Nycomed Searle	06 May 1994	DU, GU, GERD	yes
Switzerland	Pantozol Zurcal	Byk AG Nycomed	06 Feb 1997 14 Feb 1997	DU, GU, GERD	yes
Tunisia	Inipomp	Synthélabo	23 May 1997	DU, GU, GERD	yes

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TABLE 1 COMMERCIAL MARKETING HISTORY OF ORAL PANTOPRAZOLE

Country	Trade Name	Company	Registration Date	Indicauons	Marketed (yes/no)
Ukraine	Kontrolok	Byk	19 June 1996 31 Jan 1997 (*H. pylori*)	DU. GU. GERD. *H. pylori*	yes
United Arab Emirates (UAE)	Pantozol	Modern Pharmac.	29 Jan 1996	DU. GU. GERD (stages 2 and 3)	yes
United Kingdom	Protium	Knoll	04 July 1996	DU. GU. GERD	yes
[redacted]					

Oral pantoprazole is registered and marketed in 56 countries. In addition, submission packages have been sent to the health authorities and registration is pending in other countries: [redacted]

APPEARS THIS WAY
ON ORIGINAL

Item 8.7.4: Commercial Marketing Experience and Foreign Regulatory Actions

Australia
Original Language