

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

22-020

PROPRIETARY NAME REVIEW(S)

CONSULTATION RESPONSE

**DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF SURVEILLANCE AND EPIDEMIOLOGY
(DMETS; White Oak 22, Mail Stop 4447)**

DATE RECEIVED: 06/09/2006	DESIRED COMPLETION DATE: 01/15/2007	OSE REVIEW #: 06-0187
DATE OF DOCUMENT: 05/12/2006	PDUFA DATE: 03/15/2007	

TO: Brian Harvey, M.D., Ph.D
Director, Division of Gastroenterology Products
HFD-180

THROUGH: Alina R. Mahmud, R.Ph., M.S., Team Leader
Denise P. Toyer, Pharm.D., Deputy Director
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FROM: Jinhee L. Jahng, Pharm.D., Safety Evaluator
Division of Medication Errors and Technical Support, HFD-420

PRODUCT NAME: <u>Protonix</u> (Pantoprazole Sodium) Delayed-release <input type="checkbox"/> <input checked="" type="checkbox"/> 40 mg	SPONSOR: Wyeth Pharmaceuticals, Inc.
NDA #: 22-020	

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RECOMMENDATIONS:

1. DMETS has no objections to the use of the proprietary name, Protonix, for the newly proposed dosage form. This is considered a tentative decision, and the firm should be notified that this name, with its associated labels and labeling, must be re-evaluated approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary or established names from the signature date of this document.
2. DMETS recommends implementation of the label and labeling recommendations outlined in Section III of this review in order to minimize potential errors with the use of this product.
3. DDMAC finds the proprietary name, Protonix, acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Diane Smith, Project Manager, at 301-796-0538.

Division of Medication Errors and Technical Support (DMETS)
Office of Surveillance and Epidemiology
White Oak 22, Mail Stop 4447
Center for Drug Evaluation and Research

PROPRIETARY NAME, LABEL, AND PACKAGING REVIEW

DATE OF REVIEW: July 14, 2006

NDA#: 22-020

NAME OF DRUG: Protonix (Pantoprazole Sodium) Delayed-release C 3

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NDA HOLDER: Wyeth Pharmaceuticals, Inc.

I. INTRODUCTION:

This consult was written in response to a request from the Division of Gastroenterology Products (HFD-180), for assessment of the proprietary name, "Protonix", regarding potential name confusion with other proprietary or established drug names. Container labels, carton and insert labeling were provided for review and comment.

The sponsor, Wyeth Pharmaceuticals, currently markets Protonix Delayed-release Tablets (NDA 20-987) which were approved February 2, 2000 for the 40 mg strength, June 12, 2001 for the 20 mg strength, and March 22, 2001 for the Protonix I.V. (NDA 20-988). Protonix Delayed-release C 3 is an extension of the Protonix product line.

PRODUCT INFORMATION

Protonix (Pantoprazole Sodium) Delayed-release C 3 is a proton pump inhibitor (PPI) that is indicated for short-term treatment of erosive esophagitis associated with gastroesophageal reflux disease (GERD), maintenance of healing of erosive esophagitis, and for pathological hypersecretory conditions including Zollinger-Ellison syndrome. The usual adult dose depends on the indication and is as follows:

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Treatment of Erosive Esophagitis

The recommended adult oral dose is 40 mg given once daily for up to 8 weeks. For those patients who have not healed after 8 weeks of treatment, an additional 8-week course of Protonix may be considered.

Maintenance of Healing of Erosive Esophagitis

The recommended adult oral dose is Protonix 40 mg, taken daily.

Pathological Hypersecretory Conditions Including Zollinger-Ellison Syndrome

The dosage of Protonix in patients with pathological hypersecretory conditions varies with the individual patient. The recommended adult starting dose is 40 mg twice daily. Dosage regimens should be adjusted to individual patient needs and should continue for as long as clinically indicated. Doses up to 240 mg daily have been administered. Some patients have been treated continuously with Protonix for more than 2 years.

Protonix contain pantoprazole sodium enteric coated granules in a 40 mg unit dose. They are available as a unit dose carton of 30.

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II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts^{1,2} as well as several FDA databases^{3,4} for existing drug names which sound-alike or look-alike to Protonix to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted⁵. The Saegis⁶ Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name Protonix. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

¹ MICROMEDEX Integrated Index, 2006, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

² Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

³ AMF Decision Support System [DSS], the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, New Drug Approvals 98-06, and the electronic online version of the FDA Orange Book.

⁴ Phonetic and Orthographic Computer Analysis (POCA)

⁵ WWW location <http://www.uspto.gov/tmdb/index.html>.

⁶ Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at www.thomson-thomson.com

1. DDMAC finds the proprietary name Protonix acceptable from a promotional perspective.
2. The Expert Panel identified four proprietary names that were thought to have the potential for confusion with Protonix. These products are listed in Table 1 (see below), along with the dosage forms available and usual dosage.

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

[REDACTED]			
Protonix	Pantoprazole Sodium Delayed-release Tablets 40 mg	40 mg by mouth daily.	SA/LA
Protonix I.V.	Pantoprazole Sodium for Injection 40 mg per vial	40 mg by intravenous infusion once daily.	
Proteinex Liquid (OTC)	Protein Supplement that contains 15 gm of Protein Hydrolysate, L-Arginine 1200 mg, L-Histidine 110 mg, L-Isoleucine 200 mg, L-Leucine 450 mg, L-Lysine 650 mg, L-Methionine 110 mg, L-Phenylalanine 350 mg, L-Threonine 300 mg	Two tablespoons by mouth daily.	SA/LA
Proteinex Tablet (OTC)	Six tablets contain 15 gm of Protein Hydrolysate, L-Arginine 1200 mg, L-Histidine 110 mg, L-Isoleucine 200 mg, L-Leucine 450 mg, L-Lysine 650 mg, L-Methionine 110 mg, L-Phenylalanine 350 mg, L-Threonine 300 mg, L-Valine 139 mg	Two tablets by mouth three times daily.	SA/LA
Protox (Orphan drug)	Poloxamer 331	-	SA/LA
*Frequently used, not all-inclusive. **L/A (look-alike), S/A (sound-alike)			

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B. AERS AND DQRS SEARCHES

Since the name "Protonix" is currently marketed, DMETS searched the FDA Adverse Event Reporting System (AERS) database for any post-marketing safety reports. The MedDRA High Level Group Term (HLGT), "Medication Error", and the established, tradename, and verbatim "Protoni%" and "Pantoprazol%" were used to perform the searches. The Drug Quality Reporting System (DQRS) database was also searched for similar reports with "Protonix". This combined search identified nineteen medication errors (n=19) associated with Protonix. The errors can be divided into the following categories: improper dose, wrong technique, wrong drug, wrong rate, and deteriorated drug error. See Appendix A for a table containing narratives of all nineteen cases.

1. Improper Dose (n=6)

Five cases (n=5) involve medication errors where the patient took two tablets (80 mg) in the 2 tablet sample pack because either they or their caregiver were led to believe that the "40 mg" meant the equivalent of 2 tablets. In all five cases, an improper dose, resulting in an overdose, was administered. As a

result, patients experienced nausea, stomach churning, nervousness, excitability, decreased appetite, "feeling sick", headaches, and stomachaches. The sponsor no longer distributes the two tablet sample pack and instead distributes a five tablet sample pack. No new cases relating to the two tablet or five tablet sample pack have since been reported, therefore, no action is warranted at this time. However, we will continue to monitor post-marketing reports of medication errors.

In a sixth case (n=1), a patient received an overdose of Protonix, but no further information was provided.

2. Wrong Technique (n=6)

Three cases (n=3) involve administering Protonix via a wrong technique (i.e. crushing of tablets) and a fourth case (n=1) implies incorrect administration. In one of these cases, the patient died of a bleeding ulcer and another patient experienced diarrhea. No outcome was discussed in the third and fourth cases. The root cause in these four cases, stated or implied, appears to be because the labels and labeling make no statement that the tablets are "delayed release". The healthcare practitioners administering Protonix, because of this knowledge deficit, are crushing the tablets. However, the sponsor has since added the term "delayed-release" on their unit dose blister packaging, therefore, no action is warranted at this time.

In the fifth case (n=1), the reporter indicates that a filter was not used during Protonix IV administration. No mention is made as to why the filter was not used. Potassium Chloride and Protonix were both administered via a Y-site, and subsequently, the patient experienced renal impairment. Similarly, the remaining reporter (n=1) states that Protonix IV is shipped in one box. However, inside the boxes are two separate packages – one that must be refrigerated, containing the drug, Protonix, and the other one that must be kept at room temperature (the IV in-line filter). Because the package guidelines require the pharmacy to separate the two boxes, inevitably, Protonix may not be dispensed with the required filter if the person dispensing the medication is unaware of the packaging configuration. Thus, no action is warranted at this time, however we will continue to monitor post-marketing reports of medication errors.

3. Wrong Drug (n=5)

Two cases (n=2) report confusion with Protonix and Protamine. In one case, the order was given verbally to the nurse as "Protamine 40 mg IVP", but interpreted by the pharmacist as "Protonix 40 mg IVP". In the other case, the patient with a gastrointestinal bleed was ordered "Protonix 40 mg IV qd". However, the illegible order was interpreted as Protamine. In both cases, the error was discovered before the final product reached the patient. The misinterpretation of the order most likely took place because both products share an overlapping dose (40 mg), dosage form (intravenous), and have similar looking names. No additional errors have been reported, therefore, no action is warranted at this time. However, we will continue to monitor post-marketing reports of medication errors.

In two cases (n=2), the reporter's state concern about the look and sound-alike potential between Protonix and Lotronex, but no actual cases of dispensing or administration of the wrong drug have been reported to date. Additionally, the prescribing status of Lotronex has changed so that only physician's who have been enrolled in GlaxoSmithKline's Prescribing Program for Lotronex, based on their understanding of the benefits and risks, should prescribe Lotronex. No additional errors have been reported, therefore, no action is warranted at this time. However, we will continue to monitor post-marketing reports of medication errors.

The remaining reporter states confusion with the Protonix 40 mg tablet and the Trileptal 150 mg tablet. "The tablets are similar in appearance and their generic nomenclature has placed these medications in close proximity on our shelves". The medications have been mixed-up when filling their unit dose medication bins. However, no other reports have been received, but we will continue to monitor post-marketing reports of medication errors.

4. Wrong Rate (n=1)

One reporter states that a Protonix drip was administered over 30 minutes instead of 24 hours, resulting in leucopenia. The patient's Zantac and Protonix were subsequently discontinued, and the patient was given Neupogen and placed on isolation. No other information was provided. The package insert does not mention preparation of a drip nor do they mention anything about administering Protonix over a period of 24 hours. No additional errors have been reported, therefore, no action is warranted at this time. However, we will continue to monitor post-marketing reports of medication errors.

5. Deteriorated Drug Error (n=1)

One case (n=1) reports that Protonix was reconstituted and admixed for more than 12 hours. However, no cause or outcome was reported [According to the package insert, the reconstituted solution may be stored for up to 6 hours at room temperature prior to further dilution and the admixed solution may be stored at room temperature and used within 24 hours from the time of initial reconstitution.]. No other reports of this nature were reported, therefore, no action is warranted at this time. However, we will continue to monitor post-marketing reports of medication errors.

C. SAFETY EVALUATOR RISK ASSESSMENT

After assessment of the medication errors identified in the AERS search, DMETS believes that the introduction of delayed-release granules dosage form of Protonix should not increase the potential for name confusion between Protonix and any of the aforementioned drug names [(Protonix Delayed-release Tablets, Protonix for Injection, Proteinex Liquid (OTC), Proteinex Tablet (OTC), and Prottox] or dosing confusion as described in the post-marketing cases. Additionally, all of the medication error cases have either been addressed or appear to be isolated events that have not taken place in the recent past. This new proposed dosage form (delayed-release granules) has the same strength and dosage regimen and will most likely help to diminish the problems reported with the crushing of the delayed-release tablets.

Since Protonix is already available in tablets, with the introduction of the delayed-release granules, the prescriber must specify which dosage form they desire to prescribe, rather than just ordering "Protonix 20 mg or 40 mg by mouth daily." The sponsor will need to educate practitioners on the introduction of this new dosage form. The inclusion of a dosage form, specifically the delayed-release granules, should help to preclude prescriptions being filled for drugs with tradenames that may look and/or sound similar to Protonix since those products are not available in a granules dosage form (i.e. proteinex and protox). Furthermore, the introduction of the delayed-release granules should not increase the potential for confusion due to similar looking tablets (Trileptal) as identified in the AERS cases. Overall, DMETS has not identified any issues that will be exacerbated by the introduction of Protonix Delayed-release [redacted], but we recommend that efforts be made to differentiate the labels and labeling between the two formulations (tablets vs. granules) in hopes of minimizing the likelihood of possible confusion. In addition, DMETS recommends that educational measures be taken to emphasize the difference between these two medications at the time of product launch.

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III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the review of the container labels, carton and insert labeling of Protonix, DMETS focused on safety issues relating to possible medication errors. DMETS has identified the following areas of improvement, which might minimize potential user error.

A. CONTAINER LABEL

1. [redacted]

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2. [redacted]

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[redacted]

]

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b(4)

3. [redacted]

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4. [redacted]

]

[redacted]

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5. [redacted]

] b(4)

B. CARTON LABELING a.k.a. [redacted] Labeling

See comment A1-A5.

C. INSERT LABELING

No comments.

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Appendix A

Receipt Date ISR#	Type of Error	Narrative
08/02/2000 3539686-2	Improper Dose	<p>Patients (number unknown) experienced headaches and stomachaches after taking double the dose of Protonix 40 mg Tablets from sample blister packs. The nurse thought that the "40 mg" printed on each blister card was the dosage strength for both tablets on the card combined (when in fact each tablet is 40 mg). The nurse had instructed the patients to take 2 tablets per dose (instead of one tablet per dose). The nurse is upset that the Package insert does not reference the sample blister carton in the "How Supplied" section.</p> <p>A Change Control, which was initiated in June of 2000, is in process for the revision to the sample packs. This will revise the blister card to state: []</p>
08/22/2000 3554840-1	Improper Dose	<p>Patients (number unknown) experienced headaches and stomachaches after taking double the dose of Protonix 40 mg Tablets from sample blister packs. The nurse thought that the "40 mg" printed on each blister card was the dosage strength for both tablets on the card combined (when in fact each tablet is 40 mg). The nurse had instructed the patients to take 2 tablets per dose (instead of one tablet per dose). The nurse is upset that the Package insert does not reference the sample blister carton in the "How Supplied" section.</p> <p>A Change Control, which was initiated in June of 2000, is in process for the revision to the sample packs. This will revise the blister card to state: []</p>
08/31/2000 3589561-2		<p>Information has been received on 19-Jul-2000 from a nurse concerning an unknown number of patients who received Protonix (pantoprazole) 80 mg daily. Indication and therapy dates were unknown. Medical history and concomitant therapies were not provided. Patients experienced headaches and stomachaches after taking double doses of Protonix from the sample blister packs. The nurse (reporter) thought that the "40 mg" printed on each blister card was the dosage strength for both tablets combined and instructed the patients to take 2 tablets/dose (80 mg daily) instead of 1 tablet/dose (40 mg daily). She was later informed by the sales representative that the tablets were 40 mg each after contacting him because some patients reported having headaches and upset stomachs. The reporter did not provide any further information regarding the events and stated that she refuses to speak with anyone regarding the situation.</p>
09/22/2000 3588571-9	Improper Dose	<p>Patient received 8 week supply of sample prescription of Protonix (pantoprazole sodium) from physician. When patient ran out of medication early and received prescription, realized pills were identical to what she'd she had been taking and realized she had been taking double dosage. She went back to physician office and received another sample to try to figure out how she made such a mistake. She had read inside instructions but had not, apparently, read note on outside of box. Pill packets read as if both tabs are the equivalent of 40 mg.</p> <p>Change labeling to reflect each tab 40 mg.</p>
12/01/2000 3642439-8	Improper Dose	<p>Information was received on 22-SEP-2000 from a female patient (age unknown) who had taken Protonix (pantoprazole) for the treatment of gastro-esophageal reflux disease. There were no concomitant medications. The patient was given a sample package of Protonix 40 mg tablets following an invasive-gastro-intestinal procedure. On an unspecified date, the patient accidentally took 80 mg (two 40 mg tablets) of Protonix instead of her prescribed 40 mg dose. She thought that the "40 mg" on the package label was the combined strength of the two tablets in the package and not the strength of each tablet. The patient stated that she was "feeling sick" as a result. The patient notified her healthcare professional who instructed her to continue taking 40 mg daily.</p>

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12/01/2000 3642442-8	Improper Dose	Information was received on 25-SEP-2000 from an 18-year-old male consumer who was taking Protonix (pantoprazole) (tablet, delayed release) 80 mg daily decreased to 40 mg daily for approximately 2 ½ weeks for Gastro-oesophageal reflux disease. Concomitant therapy included Zantac. Medical history was not provided. The caller reported he started Protonix 80 mg once daily by mistake ("sample pack said 40 mg but had 2 pills"). Caller stated that his symptoms of "nausea and stomach churning were relieved but his mouth started to water a lot, he was very nervous, and experienced decreased appetite". His physician advised him to take directed Protonix dose of 40 mg daily. Patient experienced nausea and stomach churning daily when receiving PROtonix 40 mg daily.
08/31/2000 3589564-8	Improper Dose	Information has been received on 24-MAY-2000 from a pharmacist concerning an unidentified patient who received an overdose (unknown dose) of Protonix (pantoprazole). It is unknown if the patient has been taking concomitant therapy. The patient experienced overdose on 24-May-2000. The outcome is unknown.
01/17/2001 3649093-X	Wrong Technique	Protonix unit dose packaging omits "delayed release tablet" on label. The bulk bottle states delayed release. RN was crushing Protonix because it did not say delayed release on unit dose packaging. See photocopy of label.
03/03/2003 4093190-4	Wrong Technique	Information was received from a pharmacy student concerning an 80-year-old female patient who received Protonix (pantoprazole) (tablet, delayed release) 40 mg daily (indication and therapy start date unknown). Medical history was not provided. Concomitant therapy included Celexa (citalopram hydrobromide), Oxybutynin, Docusate, and Risperdal (risperidone). The patient experienced diarrhea (diarrhea NOS) while receiving crushed Protonix tablets. Pantoprazole therapy continues.
04/22/2005 4645873-2	Wrong Technique	Information was received from a healthcare professional regarding her 79-year-old mother who received Protonix (pantoprazole tablet, delayed release) therapy and experienced diarrhea, had not been eating, looked like she had lost weight, and had black stools. "Protonix was being crushed and administered in applesauce". The patient died from a bleeding ulcer. MEDICAL HISTORY: The patient's concurrent illnesses include hypothyroidism, hypertension and constipation with a past history of ulcer haemorrhage (Feb-2005), rectal haemorrhage (Feb-2005) and blood pressure decreased (Feb-2005). The bleeding ulcer was cauterized and the patient was subsequently transferred to a nursing home. PRODUCT DETAILS: Indication for Protonix was bleeding ulcer. Therapy began on 11-Mar-2005 ("or sooner") and was discontinued on 04-Apr-2005. Dose regimen was not provided. CONCOMITANT THERAPY: Concomitant therapy included Levothyroxine, Sular (nisoldipine), Multivitamins (ascorbic acid/ergocalciferol/folic acid/nicotinamide/panthenol/retinol/riboflavin/thiamine hydrochloride) and Stool Softener (docusate sodium). EVENT DETAILS: The pharmacist reported that her mother died from a bleeding ulcer coincident with the use of Protonix. Protonix and the patient's other medications were "being crushed and administered in applesauce" (medication error) by the nursing home staff. The patient experienced diarrhea (diarrhea) of unknown duration while in the nursing home. She had black stools (Faeces discoloured) on 31-Mar-2005. The reporter requested an occult blood test while at the nursing home on <input type="checkbox"/> but was told the black stools were due to iron. The reporter later found out that her mother was not taking an iron supplement. The occult blood test was never done and the patient "had no bowel movement after 31-Mar-2005" It was also reported that "it looked like her mother had lost weight" (weight decreased) after being transferred to the last nursing home but the staff would not weight her and claimed that she had gained weight. The nursing home staff also told the reporter that her mother had not been eating (anorexia). Her mother died on <input type="checkbox"/> and it was "determined by autopsy that she bled to death as a result of a bleeding ulcer (ulcer haemorrhage)". She died at the nursing home during the night and the reporter stated that the staff had not checked on her, mother. The autopsy cause of death was ulcer haemorrhage.
05/04/2005 4654680-6	Wrong Technique?	4 errors have been made because the "Delayed-release Tablets" is in small print under the generic name. The product should be Protonix DR 20 mg to avoid errors. Many nurses do not realize these are delayed release tabs. They think they (Protonix) are plain tablets.

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05/06/2003 4107960-7	Wrong Technique	The patient's experience was considered medically important. Information has been received from a pharmacist concerning a male patient (born in 1949) who had been receiving Protonix (pantoprazole) (injection) 80 mg twice daily beginning 22-Apr-2003 and ended 24-Apr-2003 for a GI bleed. An additional suspect medication included potassium chloride. Concomitant therapy included potassium chloride. Concomitant therapy included Levaquin (levofloxacin) and "colon prep". Medical history included gastrointestinal haemorrhage NOS. The reporter stated that the patient experienced renal impairment (renal impairment NOS) coincident with Protonix therapy. After two days of Protonix therapy, the patient's lab values were "remarkably" raised. Lab values on 22-Apr-2003 were as follows: blood creatinine 0.8, blood urea 6, and potassium 4.1. Lab values on 24-Apr-2003 were as follows: blood creatinine 4, blood urea 42, and potassium 5.9. The reporter also noted the patient was given potassium chloride coincident with Protonix administration through a Y-site. The reporter stated nursing did not use a filter during Protonix administration (medication error). The reporter inquired if administration of potassium chloride with Protonix, without a filter, could have caused the renal impairment and/or the concomitant use of the medications cause a precipitate (infusion related reaction). The reporter refused to give physician information (HIPPA). The reporter was not aware of treatment or outcome information at the time of this report.
08/23/2001 3782006-9	Wrong Technique	Wyeth-Ayerst new Protonix-IV is shipped in one box. Inside the box are 2 separate packages, one that must be refrigerated (the drug Protonix), and one that must be kept at room temperature (the IV in-line filter). Wyeth reps told reporter that the FDA required that the filters be shipped with the drug. This is totally unprecedented in that other IV products already on the market that require filtering, are not forced to provide the filter. If the FDA's idea was to insure filtering, it fails because the pharmacy must separate these packages. If a pharmacy fails to separate the two items, they are violating package guidelines. They have heard that at least one wholesaler refuses to stock the item because of this dilemma.
11/15/2001 3832538-X	Wrong Drug	The pharmacists have noticed that the following medication mix-up has been occurring in the filling our unit dose medication bins. We have recently added Protonix as our sole source PPI and shortly afterward have observed that bins have been filled with Protonix 40 mg Trileptal 150 mg tablets. The tablets are similar in appearance and their generic nomenclature has placed these medications in close proximity on our shelves. This observation has been passed on to our sales representative.
12/19/2000 3640654-0	Wrong Drug	Protonix (proton pump inhibitor) and Lotronex – for irritable bowel – sound alike and could easily be confused in a verbal order.
09/28/200 3592455-X	Wrong Drug	Lotronex and Protonix likely to be confused (both for stomach).
03/13/2002 3895560-3	Wrong Drug	Pt with GI bleed is ordered Protonix 40 mg IV qd. Since the handwriting was sloppy, the protonix look like protamine 40 mg IV qd. Caught in Pharmacy dept. before order verified. Orders put into computer system by unit secretary. Order faxed to pharmacy for verification and dispensing. Upon order review, pharmacist caught mistake.
01/30/2004 4284451-4	Wrong Drug	A verbal order was written by a nurse for Protamine 40 mg IVP. The pharmacist interpreted the order as Protonix 40 mg IVP. When the pharmacist called the nurse to tell her that we would be sending a piggy back and that Protonix was not given push, the nurse clarified the order as Protamine.
11/28/2001 3830456-4	Wrong Rate	Patient administered 96 mg of Protonix over 30 minutes instead of 24 hours. This resulted in Leucopenia. Patient's Zantac and Protonix were discontinued and patient was given Neupogen and placed on isolation. WBC went from 4600 down to 900 Plts went from 86,000 down to 30,000.

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10/22/2001 3813043-3	Deteriorated Drug Error	Information has been received from a gastroenterologist concerning an 81-year-old female patient who was administered Protonix (pantoprazole) (injection) 8 mg per hour intravenously (from 00-JUL-2001 to continues) for treatment of gastrointestinal bleed. Medical history was not provided. Concomitant therapy included Versed (midazolam hydrochloride), Cordarone (amiodarone hydrochloride), Diruil (chlorothiazide), Aspirin (acetylsalicylic acid), Dopamine, Lasix (furosemide), Levbid (hyoscymaine sulfate), Cleocin (clindamycin hydrochloride), Levaquin (levofloxacin), Carafate (sucralfate), Calcium Gluconate, Hydroxyzine, TPN (nicotinamide/pyridoxine hydrochloride/tyrosine), and Neosynephrine (phenylephrine hydrochloride). Pharmacist reported, on 08-JUL-2001, patient received intravenous Protonix that had been reconstituted and admixed for more than 12 hours. No symptoms have been reported.
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Jinhee Jahng
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Alina Mahmud
9/22/2006 03:25:14 PM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
9/22/2006 03:39:32 PM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
9/22/2006 03:50:47 PM
DRUG SAFETY OFFICE REVIEWER

REQUEST FOR CONSULTATION

TO (Office/Division):
Division of Medication Errors and Technical Support
Attention: Diane Smith, RPM
W.O., Room 4421; x60538

FROM (Name, Office/Division, and Phone Number of Requestor):
Division of Gastroenterology Products
HFD-180
Mary M. Lewis, RPM
W.O. Room 5102, x60941

DATE
June 9, 2006

IND NO.

NDA NO.
22-020

TYPE OF DOCUMENT
New NDA Labeling

DATE OF DOCUMENT
May 12, 2006

NAME OF DRUG
Protonix (pantoprazole sodium) Delayed Release
C 7

PRIORITY CONSIDERATION
Standard

CLASSIFICATION OF DRUG
Propton Pump Inhibitor

DESIRED COMPLETION DATE
January 15, 2007

NAME OF FIRM: Wyeth

REASON FOR REQUEST

I. GENERAL

- | | | |
|--|--|--|
| <input type="checkbox"/> NEW PROTOCOL | <input type="checkbox"/> PRE-NDA MEETING | <input type="checkbox"/> RESPONSE TO DEFICIENCY LETTER |
| <input type="checkbox"/> PROGRESS REPORT | <input type="checkbox"/> END-OF-PHASE 2a MEETING | <input type="checkbox"/> FINAL PRINTED LABELING |
| <input type="checkbox"/> NEW CORRESPONDENCE | <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> LABELING REVISION |
| <input type="checkbox"/> DRUG ADVERTISING | <input type="checkbox"/> RESUBMISSION | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE |
| <input type="checkbox"/> ADVERSE REACTION REPORT | <input type="checkbox"/> SAFETY / EFFICACY | <input type="checkbox"/> FORMULATIVE REVIEW |
| <input type="checkbox"/> MANUFACTURING CHANGE / ADDITION | <input type="checkbox"/> PAPER NDA | <input checked="" type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> MEETING PLANNED BY | <input type="checkbox"/> CONTROL SUPPLEMENT | |

II. BIOMETRICS

- | | |
|---|---|
| <input type="checkbox"/> PRIORITY P NDA REVIEW | <input type="checkbox"/> CHEMISTRY REVIEW |
| <input type="checkbox"/> END-OF-PHASE 2 MEETING | <input type="checkbox"/> PHARMACOLOGY |
| <input type="checkbox"/> CONTROLLED STUDIES | <input type="checkbox"/> BIOPHARMACEUTICS |
| <input type="checkbox"/> PROTOCOL REVIEW | <input type="checkbox"/> OTHER (SPECIFY BELOW): |
| <input type="checkbox"/> OTHER (SPECIFY BELOW): | |

III. BIOPHARMACEUTICS

- | | |
|--|--|
| <input type="checkbox"/> DISSOLUTION | <input type="checkbox"/> DEFICIENCY LETTER RESPONSE |
| <input type="checkbox"/> BIOAVAILABILITY STUDIES | <input type="checkbox"/> PROTOCOL - BIOPHARMACEUTICS |
| <input type="checkbox"/> PHASE 4 STUDIES | <input type="checkbox"/> IN-VIVO WAIVER REQUEST |

IV. DRUG SAFETY

- | | |
|--|--|
| <input type="checkbox"/> PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL | <input type="checkbox"/> REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY |
| <input type="checkbox"/> DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES | <input type="checkbox"/> SUMMARY OF ADVERSE EXPERIENCE |
| <input type="checkbox"/> CASE REPORTS OF SPECIFIC REACTIONS (List below) | <input type="checkbox"/> POISON RISK ANALYSIS |
| <input type="checkbox"/> COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP | |

V. SCIENTIFIC INVESTIGATIONS

- | | |
|-----------------------------------|--------------------------------------|
| <input type="checkbox"/> CLINICAL | <input type="checkbox"/> NONCLINICAL |
|-----------------------------------|--------------------------------------|

COMMENTS / SPECIAL INSTRUCTIONS: NDA 22-020 Protonix (pantoprazole sodium) D.R. C 7 40 mg was submitted electronically and is a 505(b)(2) application. It may be found in the EDR entitled N022020, Protonix Delayed Release C 7 Wyeth Pharms Inc., document date: 12-May-2006 N 00 in the labeling folder in the FDA Regional Information folder. The PDUFA goal date is March 15, 2007. Please review the package insert; and carton and container if appropriate. Thank you.

SIGNATURE OF REQUESTOR
Mary M. Lewis, RPM x60941

METHOD OF DELIVERY (Check one)
 DFS EMAIL MAIL HAND

PRINTED NAME AND SIGNATURE OF RECEIVER

PRINTED NAME AND SIGNATURE OF DELIVERER

b(4)

b(4)

**This is a representation of an electronic record that was signed electronically and
this page is the manifestation of the electronic signature.**

/s/

Mary Lewis
6/9/2006 02:25:48 PM