

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPROVAL PACKAGE FOR:**

**APPLICATION NUMBER**

**NDA 21-566**

**Administrative/Correspondence Reviews**

Lansoprazole for injection  
Patent Information  
TAP-02-001036-1.0

### Patent Information

TAP Pharmaceutical Products Inc. (TAP) certifies that the drug, lansoprazole, is claimed in U.S. Patents as listed below. Takeda Chemical Industries, Ltd., of Japan has licensed lansoprazole as covered by these patents to TAP.

U.S. Patent No.	Expiration Date	Coverage
4,628,098	05/10/09	Compound



\_\_\_\_\_  
Paul Yasger  
Counsel  
TAP Pharmaceutical Products Inc.

12/3/02  
Date

Lansoprazole for injection  
Patent Certification  
TAP-02-001037-1.0

### **Patent Certification**

The patent certification for lansoprazole for injection is included in the patent information section of this NDA

Appears This Way  
On Original

EXCLUSIVITY SUMMARY for NDA # NDA 21-566 SUPPL # -----

Trade Name Prevacid IV

Generic Name (lansoprazole)

Applicant Name Tap Pharmaceutical Products, Inc.  
HFD- 180

Approval Date 05/27/04

**PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?**

1. An exclusivity determination will be made for all original applications, but only for certain supplements. Complete Parts II and III of this Exclusivity Summary only if you answer "YES" to one or more of the following questions about the submission.

a) Is it an original NDA? YES/ x / NO /     /

b) Is it an effectiveness supplement? YES /     / NO / x /

If yes, what type(SE1, SE2, etc.)? -----

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "NO.")

YES /     x     / NO /     /

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES /\_\_/  
NO /\_x\_/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

e) Has pediatric exclusivity been granted for this Active Moiety?

YES /\_\_/  
NO /\_x\_/

**IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.**

2. Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule previously been approved by FDA for the same use? (Rx to OTC Switches should be answered No - Please indicate as such).

YES /\_\_/  
NO /\_x\_/

If yes, NDA # \_\_\_\_\_ Drug Name

**IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.**

3. Is this drug product or indication a DESI upgrade?

YES /\_\_/  
NO /\_x\_/

**IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9 (even if a study was required for the upgrade).**

**PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES**  
(Answer either #1 or #2, as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES / x / NO / \_\_\_ /

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA # 20-406 Prevacid (lansoprazole)Delayed-Release Capsules

NDA # 21-281 Prevacid (lansoprazole)for Oral Suspension

NDA # 21-428 Prevacid Solutab(lansoprazole)Orally Disintegrating Tablet

2. Combination product.

If the product contains more than one active moiety (as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES /\_\_\_/      NO /\_\_\_/

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA #

NDA #

NDA #

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9. IF "YES," GO TO PART III.

**PART III: THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS**

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2, was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES /\_x\_/      NO /\_\_\_/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON Page 9.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement

or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

For the purposes of this section, studies comparing two products with the same ingredient(s) are considered to be bioavailability studies.

- (a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES // NO //

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON Page 9:**

- (b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES // NO //

- (1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES // NO //

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES /\_\_\_/ NO /\_x\_/

If yes, explain:

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Investigation #1, Study # M01-308

Investigation #2, Study #

Investigation #3, Study #

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

(a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /\_\_\_/ NO /\_x\_/

Investigation #2 YES /\_\_\_/ NO /\_\_\_/

Investigation #3 YES /\_\_\_/ NO /\_\_\_/

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

NDA # \_\_\_\_\_ Study #  
NDA # \_\_\_\_\_ Study #  
NDA # \_\_\_\_\_ Study #

- (b) For each investigation identified as "essential to the approval," does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1                    YES /\_\_\_/                    NO /\_x\_/

Investigation #2                    YES /\_\_\_/                    NO /\_\_\_/

Investigation #3                    YES /\_\_\_/                    NO /\_\_\_/

If you have answered "yes" for one or more investigations, identify the NDA in which a similar investigation was relied on:

NDA # \_\_\_\_\_ Study #  
NDA # \_\_\_\_\_ Study #  
NDA # \_\_\_\_\_ Study #

- (c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Investigation #\_\_, Study # M01-308

Investigation #\_\_, Study #

Investigation #\_\_, Study #

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

(a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1 !  
!  
IND # 41,938 YES /x/ NO /\_\_\_/ Explain:  
!  
!  
!  
!

Investigation #2 !  
!  
IND # \_\_\_ YES /\_\_\_/ NO /\_\_\_/ Explain:  
!  
!  
!  
!

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1 !  
!  
YES /\_\_\_/ Explain \_\_\_\_\_ ! NO /\_\_\_/ Explain \_\_\_\_\_  
!  
\_\_\_\_\_  
!  
\_\_\_\_\_  
!  
\_\_\_\_\_

Investigation #2 !  
!  
YES /\_\_\_/ Explain \_\_\_\_\_ ! NO /\_\_\_/ Explain \_\_\_\_\_  
!  
\_\_\_\_\_  
!  
\_\_\_\_\_  
!  
\_\_\_\_\_

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /\_\_\_/            NO /\_x\_/

If yes, explain: \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

Melissa Furness  
Signature of Preparer

05/27/04  
Date

Title: Regulatory Health Project Manager

Dr. Robert Justice  
Signature of Office or Division Director

05/27/04  
Date

cc:  
Archival NDA  
HFD- /Division File  
HFD- /RPM  
HFD-093/Mary Ann Holovac  
HFD-104/PEDS/T.Crescenzi

Form OGD-011347  
Revised 8/7/95; edited 8/8/95; revised 8/25/98, edited 3/6/00

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

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Joyce Korvick  
6/9/04 12:42:18 PM

## PEDIATRIC PAGE

(Complete for all APPROVED original applications and efficacy supplements)

NDA/BLA #: NDA 21-566 Supplement Type (e.g. SE5):        Supplement Number:       

Stamp Date: 01/12/04 (2nd cycle) Action Date: 07/12/04

HFD-180 Trade and generic names/dosage form: Prevacid IV (lansoprazole) for Injection

Applicant: Tap Pharmaceutical Product, Inc. Therapeutic Class:       

Indication(s) previously approved:       

Each approved indication must have pediatric studies: Completed, Deferred, and/or Waived.

Number of indications for this application(s): 1

Indication #1: when patients are unable to take the oral formulations, PREVACID I.V. for Injection is indicated as an alternative for the short-term treatment (up to 7 days) of all grades of erosive esophagitis

Is there a full waiver for this indication (check one)?

- Yes: Please proceed to Section A.
- No: Please check all that apply:        Partial Waiver  Deferred  Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

### Section A: Fully Waived Studies

Reason(s) for full waiver: Please note that a waiver was not granted prior to the Pediatric Rule being challenged in court.

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Other:

*If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.*

### Section B: Partially Waived Studies

Age/weight range being partially waived:

Min        kg        mo.        yr.        Tanner Stage         
Max        kg        mo.        yr.        Tanner Stage       

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed

Other: \_\_\_\_\_

*If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.*

**Section C: Deferred Studies**

Age/weight range being deferred:

Min \_\_\_\_\_ kg \_\_\_\_\_ mo. \_\_\_\_\_ yr. 17 Tanner Stage \_\_\_\_\_  
Max \_\_\_\_\_ kg \_\_\_\_\_ mo. \_\_\_\_\_ yr. < 1 Tanner Stage \_\_\_\_\_

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- X Adult studies ready for approval
- X Formulation needed

Other: \_\_\_\_\_

Date studies are due (mm/dd/yy): \_\_\_\_\_

*If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.*

**Section D: Completed Studies**

Age/weight range of completed studies:

Min \_\_\_\_\_ kg \_\_\_\_\_ mo. \_\_\_\_\_ yr. \_\_\_\_\_ Tanner Stage \_\_\_\_\_  
Max \_\_\_\_\_ kg \_\_\_\_\_ mo. \_\_\_\_\_ yr. \_\_\_\_\_ Tanner Stage \_\_\_\_\_

Comments:

*If there are additional indications, please proceed to Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.*

**Comments Regarding Sections C and D**

We note that the firm has submitted pediatric studies for ages 12-17 with NDA 20-406/S-057, completed studies for ages 1-11 (NDA 20-406/S-047), and plans to initiate studies in children less than 1 year of age after the completion of their required rat toxicity study. For Prevacid I.V. (lansoprazole) for Injection, a bridging PK (pharmacokinetic) study will be needed in children due to our concerns regarding the basic nature of this formulation of Prevacid.

This page was completed by:

{See appended electronic signature page}

NDA 21-  
Page 3

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**Regulatory Project Manager**

cc: NDA

HFD-950/ Terrie Crescenzi

HFD-960/ Grace Carmouze

(revised 9-24-02)

**FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, PEDIATRIC TEAM, HFD-960  
301-594-7337**

**Attachment A**

(This attachment is to be completed for those applications with multiple indications only.)

Indication #2: \_\_\_\_\_

Is there a full waiver for this indication (check one)?

- Yes: Please proceed to Section A.
- No: Please check all that apply: \_\_\_ Partial Waiver \_\_\_ Deferred \_\_\_ Completed

NOTE: More than one may apply

Please proceed to Section B, Section C, and/or Section D and complete as necessary.

**Section A: Fully Waived Studies**

Reason(s) for full waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Other: \_\_\_\_\_

*If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please see Attachment A. Otherwise, this Pediatric Page is complete and should be entered into DFS.*

**Section B: Partially Waived Studies**

Age/weight range being partially waived:

Min \_\_\_\_\_ kg \_\_\_\_\_ mo. \_\_\_\_\_ yr. \_\_\_\_\_ Tanner Stage \_\_\_\_\_  
Max \_\_\_\_\_ kg \_\_\_\_\_ mo. \_\_\_\_\_ yr. \_\_\_\_\_ Tanner Stage \_\_\_\_\_

Reason(s) for partial waiver:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: \_\_\_\_\_

*If studies are deferred, proceed to Section C. If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS*

**Section C: Deferred Studies**

Age/weight range being deferred:

Min \_\_\_\_\_ kg \_\_\_\_\_ mo. \_\_\_\_\_ yr. \_\_\_\_\_ Tanner Stage \_\_\_\_\_  
Max \_\_\_\_\_ kg \_\_\_\_\_ mo. \_\_\_\_\_ yr. \_\_\_\_\_ Tanner Stage \_\_\_\_\_

Reason(s) for deferral:

- Products in this class for this indication have been studied/labeled for pediatric population
- Disease/condition does not exist in children
- Too few children with disease to study
- There are safety concerns
- Adult studies ready for approval
- Formulation needed
- Other: \_\_\_\_\_

Date studies are due (mm/dd/yy): \_\_\_\_\_

*If studies are completed, proceed to Section D. Otherwise, this Pediatric Page is complete and should be entered into DFS.*

**Section D: Completed Studies**

Age/weight range of completed studies:

Min \_\_\_\_\_ kg \_\_\_\_\_ mo. \_\_\_\_\_ yr. \_\_\_\_\_ Tanner Stage \_\_\_\_\_  
Max \_\_\_\_\_ kg \_\_\_\_\_ mo. \_\_\_\_\_ yr. \_\_\_\_\_ Tanner Stage \_\_\_\_\_

Comments:

*If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS.*

This page was completed by:

*{See appended electronic signature page}*

\_\_\_\_\_  
Regulatory Project Manager

cc: NDA  
HFD-960/ Terrie Crescenzi  
(revised 1-18-02)

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, PEDIATRIC TEAM, HFD-960  
301-594-7337

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

-----  
Melissa Furness

6/2/04 03:11:56 PM

Lansoprazole for injection  
Debarment Certification  
TAP-02-001034-1.0

### Debarment Certification

I hereby certify that TAP Pharmaceutical Products Inc. did not and will not use, in any capacity, the services of any person debarred under subsection (a) or (b) [Section 306(a) or (b) in connection with this application (NDA 21-566).



Harold Cohen  
Director of Quality Assurance  
TAP Pharmaceutical Products Inc.

11/7/02  
Date

5 Page(s) Withheld

\_\_\_\_\_ § 552(b)(4) Trade Secret / Confidential



\_\_\_\_\_ § 552(b)(5) Deliberative Process

\_\_\_\_\_ § 552(b)(5) Draft Labeling



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation III

FACSIMILE TRANSMITTAL SHEET

DATE:

To: Donna Helms	From: Melissa Furness
Company: TAP	Division of Gastrointestinal and Coagulation Drug Products
Fax number: 847-582-2880	Fax number: 301-443-9285
Phone number: 847-582-4922	Phone number: 301-827-7450
Subject: NDA 21-566 Action Letter	
Total no. of pages including cover: 23	

Comments:

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TAP Pharmaceutical Products Inc.  
Regulatory Affairs  
675 N. Field Drive  
Lake Forest, Illinois 60045

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## Facsimile Cover Sheet

<b>To:</b>	Ms. Melissa Furness	<b>From:</b>	Nancianne Knipfer
<b>Co:</b>		<b>Dept:</b>	T85 (Regulatory Affairs)
<b>Fax:</b>	(301) 443-9285	<b>Fax:</b>	(847) 582-2880
<b>Phone:</b>	(301) 827-7450	<b>Phone:</b>	(847) 582-2193
<b>Pages:</b>	4	<b>Date:</b>	5/27/04
<b>Re:</b>		<b>CC:</b>	



TAP PHARMACEUTICAL PRODUCTS INC.

675 North Hickory Drive  
Lake Forest, IL 60045

**NDA AMENDMENT  
Labeling**

May 27, 2004

Robert Justice, M.D.  
Director  
Division of Gastrointestinal and Coagulation Drug Products, HFD-180  
Document Control Room 8B-45  
Center for Drug Evaluation and Research  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

**RE: PREVACID® I.V. (lansoprazole) for Injection  
NDA 21-566/Amendment 019**

Dear Dr. Justice,

The sponsor, TAP Pharmaceutical Products Inc. (TAP), submits this amendment to the above pending New Drug Application under the provisions of 21 CFR § 314.60. The purpose of this amendment is to respond to the Division's facsimile dated May 27, 2004.

TAP hereby agrees to all labeling changes as requested in the facsimile for the carton, peel-off sticker, filter pack labeling and package insert. TAP agrees to revise the carton, filter pack and peel-off sticker labeling at the second printing and the package insert at the first printing.

If you have any questions, please contact me at the number below.

Sincerely,

A handwritten signature in cursive script that reads 'Nancianne Knipfer'.

Nancianne Knipfer, Ph.D.  
Regulatory Product Manager  
847-582-2193  
847-582-2880 (fax)

<b>DEPARTMENT OF HEALTH AND HUMAN SERVICES</b> <b>FOOD AND DRUG ADMINISTRATION</b>		Form Approved: OMB No. 0910-0338 Expiration Date: August 31, 2005 See OMB Statement on page 2.	
<b>APPLICATION TO MARKET A NEW DRUG, BIOLOGIC,</b> <b>OR AN ANTIBIOTIC DRUG FOR HUMAN USE</b> <i>(Title 21, Code of Federal Regulations, Parts 314 &amp; 601)</i>		<b>FOR FDA USE ONLY</b>	
		APPLICATION NUMBER	
<b>APPLICANT INFORMATION</b>			
NAME OF APPLICANT TAP Pharmaceutical Products Inc.		DATE OF SUBMISSION 5/27/04	
TELEPHONE NO. (Include Area Code) (847) 582-2193		FACSIMILE (FAX) Number (Include Area Code) (847) 582-2880	
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 675 North Field Drive Lake Forest, IL 60045		AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE Not applicable.	
<b>PRODUCT DESCRIPTION</b>			
NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (if previously issued) NDA 21-566			
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) lansoprazole		PROPRIETARY NAME (trade name) IF ANY PREVACID® I.V. (lansoprazole) for Injection	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (if any) 2[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]benzimidazole		CODE NAME (if any) AG-1749, A-65006	
DOSAGE FORM: I.V. Infusion	STRENGTHS: 30 mg	ROUTE OF ADMINISTRATION: I.V.	
(PROPOSED) INDICATION(S) FOR USE: Short-term treatment (up to 7 days) of erosive esophagitis.			
<b>APPLICATION DESCRIPTION</b>			
APPLICATION TYPE (check one) <input checked="" type="checkbox"/> NEW DRUG APPLICATION (CDA, 21 CFR 314.50) <input type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)			
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input checked="" type="checkbox"/> 505 (b)(1) <input type="checkbox"/> 505 (b)(2)			
IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION			
Name of Drug _____		Holder of Approved Application _____	
TYPE OF SUBMISSION (check one) <input type="checkbox"/> ORIGINAL APPLICATION <input checked="" type="checkbox"/> AMENDMENT TO PENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input type="checkbox"/> OTHER			
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____			
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> Prior Approval (PA)			
REASON FOR SUBMISSION Respond to the Division's facsimile dated May 27, 2004			
PROPOSED MARKETING STATUS (check one) <input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)			
NUMBER OF VOLUMES SUBMITTED <u>1</u>		THIS APPLICATION IS <input checked="" type="checkbox"/> PAPER <input type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC	
ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.) Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready. Not applicable.			
Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application) Not applicable.			

## This application contains the following items: (Check all that apply)

<input type="checkbox"/>	1. Index
<input checked="" type="checkbox"/>	2. Labeling (check one) <input checked="" type="checkbox"/> Draft Labeling <input type="checkbox"/> Final Printed Labeling
<input type="checkbox"/>	3. Summary (21 CFR 314.50 (c))
<input type="checkbox"/>	4. Chemistry section
<input type="checkbox"/>	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)
<input type="checkbox"/>	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (a)) (Submit only upon FDA's request)
<input type="checkbox"/>	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)
<input type="checkbox"/>	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)
<input type="checkbox"/>	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)
<input type="checkbox"/>	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))
<input type="checkbox"/>	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)
<input type="checkbox"/>	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)
<input type="checkbox"/>	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)
<input type="checkbox"/>	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)
<input type="checkbox"/>	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)
<input type="checkbox"/>	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))
<input type="checkbox"/>	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (i)(2)(A))
<input type="checkbox"/>	15. Establishment description (21 CFR Part 600, if applicable)
<input type="checkbox"/>	16. Debarment certification (FD&C Act 306 (k)(1))
<input type="checkbox"/>	17. Field copy certification (21 CFR 314.50 (l)(3))
<input type="checkbox"/>	18. User Fee Cover Sheet (Form FDA 3397)
<input type="checkbox"/>	19. Financial Information (21 CFR Part 54)
<input type="checkbox"/>	20. OTHER (Specify)

## CERTIFICATION

I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:

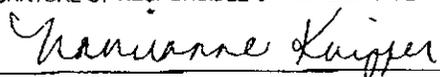
1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.
2. Biological establishment standards in 21 CFR Part 600.
3. Labeling regulations in 21 CFR Parts 201, 606, 810, 660, and/or 809.
4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.
5. Regulations on making changes in application in FD&C Act section 506A, 21 CFR 314.71, 314.72, 314.97, 314.99, and 601.12.
6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.
7. Local, state and Federal environmental impact laws.

If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.

The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.

Warning: A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.

SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT



TYPED NAME AND TITLE

Nancianne Knipfer, Ph.D.  
Regulatory Product Manager

DATE:

5/27/04

ADDRESS (Street, City, State, and ZIP Code)

675 North Field Drive, Lake Forest, IL 60045

Telephone Number

( 847 ) 582-2193

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Food and Drug Administration  
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Food and Drug Administration

CDER (HFD-99)  
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Rockville, MD 20852

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Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation III

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**FACSIMILE TRANSMITTAL SHEET**

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**DATE: 05/27/04**

<b>To:</b> Nancy Knipfer, Ph.D.	<b>From:</b> Melissa Hancock Furness
<b>Company:</b> Tap Pharmaceuticals, Inc.	Division of Gastrointestinal and Coagulation Drug Products
<b>Fax number:</b> 847-582-2880	<b>Fax number:</b> 301-443-9285
<b>Phone number:</b> 847-582-2193	<b>Phone number:</b> 301-827-7450
<b>Subject:</b> NDA 21-566 – Labeling Comments	

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**Total no. of pages including cover: 3**

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**Comments:**

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 827-7450. Thank you.

The Agency has the following additional comments regarding your proposed label for NDA 21-566:

A. CARTON LABELING

Include the instructions on the "FRONT PANEL" to read, "After reconstitution with 5 mL of Sterile Water for Injection, USP, the resulting solution will contain lansoprazole 6 mg/mL (30 mg/5 mL)."

B. FILTER PACK LABELING

1. Revise the statement [ ] to read "In-line filter" and increase its prominence. Additionally, the brand name and size of the filter (PALL Supor 1.2  $\mu$ m) should appear in parenthesis immediately following the statement "In-line filter."
2. Decrease the prominence of the statement "Prevacid IV (lansoprazole) for Injection" and precede this statement with "For use with."
3. Revise the statement "Caution: Federal (USA) law restricts...." To read "Rx Only."

C. PEEL-OFF STICKER

Revise the statement [ ] to read "IN-LINE FILTER MUST BE USED."

D. PACKAGE INSERT

1. Provide the instructions for use to priming the filter in the DOSAGE AND ADMINISTRATION section of the Package Insert in case the labeling is lost or misplaced.

Please Note that the Agency would like for you to agree to make the above changes (A-C) at your second printing and change (D) prior to your first printing.

Please send us a response via facsimilie if you agree to these changes as soon as possible.

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/s/

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Melissa Furness  
5/27/04 10:01:00 AM  
CSO

Melissa Furness  
5/27/04 10:03:07 AM  
CSO

05/18/04

**MEMORANDUM**

**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
FOOD AND DRUG ADMINISTRATION  
Center for Drug Evaluation and Research**

---

**DATE:** 5/18/2004

**FROM:** Joyce A Korvick, MD, MPH  
DGCDP/ODE III

**SUBJECT:** Director (Deputy) Summary Approval Comments  
NDA 21-566

**APPLICANT:** TAP Pharmaceutical Products, INC.

**DRUG:** Prevacid<sup>TM</sup> (lansoprazole) Injection

**DIVISION RECOMMENDATION:**

The Division recommends approval of Prevacid<sup>TM</sup> (lansoprazole) Injection to be used when patients are unable to take the oral formulations as an alternative for the short-term treatment (up to 7 days) of all grades of erosive esophagitis. Once the patient is able to take medications orally, therapy can be switched to an oral formulation of Prevacid for a total of 6 to 8 weeks. The safety and efficacy of Prevacid IV for Injection as an initial treatment have not been demonstrated. This formulation will be co-packaged with an in-line filter until CMC reformulation issues are addressed. Labeling issues have been resolved (see comments below).

In February of 2004 the division had completed its first review of this NDA submission and recommended that Prevacid<sup>TM</sup> (lansoprazole) Injection be made approvable pending resolution of chemistry compatibility issues. In addition the clinical reviewers recommend against including pediatric labeling for this product due to the high pH of the infused solution and the lack of actual safety data in children, specifically adverse events related to the infusion site.

**Regulatory History:**

Prevacid is currently approved as an oral formulation for the treatment of the following: short-term treatment of active duodenal ulcer; *H. pylori* eradication to reduce the risk of duodenal ulcer recurrence; maintenance of healed duodenal ulcers; short-term treatment of active benign gastric ulcer; healing of non-steroid anti-inflammatory drugs (NSAID) associated gastric ulcer; risk reduction of NSAID- associated gastric ulcer; gastroesophageal reflux disease (GERD); short-term treatment of symptomatic GERD; short-term treatment of erosive esophagitis (EE); maintenance of healing of EE; and pathological hypersecretory conditions including Zollinger-Ellison syndrome. In addition it is labeled for use in children from age 1 year to 11 years of age.

The current application is seeking approval for the indication of the short-term treatment (up to 7 days) of all grades of erosive esophagitis as an alternative when patients are unable to take oral formulations.

Prevacid is the second drug in its class (proton pump inhibitors) to submit an application for intravenous formulation. Protonix is currently marketed in intravenous formulation with a co-packaged in-line filter.

**Pharmacology/ Toxicology:**

The animal toxicity studies, which were submitted, had findings that were similar to those of the oral formulations. There were no new toxicity findings in the intravenous toxicity studies.

**Biopharmaceutics:**

The major data submitted in support of this NDA came from Clinical Pharmacology studies. The applicant submitted 4 studies reporting PK and PD (acid suppression) data from crossover studies of the oral versus the IV route in healthy volunteers. According to the Biopharmaceutics review, overall, equivalent dose of 30-mg lansoprazole administered by IV 30-minute infusion every day for 7 days produces similar gastric acid output suppression compared to oral lansoprazole. "Intravenous (IV) administration of lansoprazole 30 mg QD resulted in higher systemic exposure [higher peak plasma concentration (C<sub>max</sub>) and the area under the plasma concentration-time curve (AUC) values] compared to that of oral lansoprazole 30 mg QD (C<sub>max</sub> increased by 155% and AUC increased by 35%). Intravenous 30-minute infusion of lansoprazole 30 mg QD showed an improvement over oral route in gastric acid output suppression with respect to BAO) (basal acid output), but not significantly different in terms of MAO (pentagastrin-stimulated maximum acid output) in patients on Day 7." None of these studies were performed in children.

The safety of the increased C<sub>max</sub> and AUC of the intravenous formulation will be discussed in the clinical section.

**Clinical:**

As was mentioned above, the major studies in support of this application were PK/PD. It was concluded that IV prevacid was similar in its action and efficacy to that of oral prevacid at the same dose (30-mg QD).

In support of the safety of this formulation the Integrated Summary of safety included 161 individuals who received IV lansoprazole. Sixty-two of these were patients with erosive esophagitis and the other 99 were healthy subjects. In addition to these patients Dr. Nair reviewed adverse events reported in 17 non-US trials. The analysis of these data demonstrated a safety profile that appeared comparable to that of the oral formulation regarding short-term use. The reviewer and team leader felt that based upon this data, the requested short-term dose of 30-mg QD was safe.

Finally, the currently approved oral formulations are administered in doses from 15 mg daily up to 12 weeks, to 30 mg 3 times daily for 14 days (in *H. pylori* treatment), to 60 mg daily for Zollinger-Ellison Syndrome. This provides for additional rationale on the safety of this product given the expected increased C<sub>max</sub> and AUC of the 30 mg IV compared to the 30-mg oral dose. In addition, lansoprazole has a short half-life and does not accumulate.

**Chemistry:**

The major area of concern in the CMC review of this formulation was that of compatibility. In the proposed labeling IV prevacid was to be reconstituted in 5 mL of Sterile Water for Injection, USP in preparation for use. Reconstitution yields a solution with a concentration of 6 mg/mL and a pH of approximately 11 that is stable when stored at 25°C. Before administration to the patient, further dilution in 50 mL of 0.9% Sodium chloride is required. This solution has a pH of approximately 10. Because of the small volume and length of the infusion (30 minutes) this high pH is unlikely to cause acid-base disturbances in adults. TAP states that this solution should not be mixed with other drugs or diluents due to incompatibilities. The proposed label provided for use only in 7 bags.

In a DR letter, the chemists requested the applicant perform additional compatibility studies in other bags with other diluents during this review cycle. The applicant finally did some additional testing with a second diluent (5% Dextrose) and additional bags. They included 7 bags from 3

IV bags. The applicant used 3 lots of each bag. It was discovered that there was a particulate that formed in the 7 bags. The applicant is currently performing Stage II testing of this particulate. The reason for particulate formation is as yet undetermined.

IV tubing is also used to deliver the IV formulation in addition to the bags. IV tubing is made out of a substance similar to that in the 7 bags and was not tested. Thus, while there was no apparent particulate formation in the 7 bags tested, it is not acceptable to

proceed with labeling bag while the same solution will have to flow through tubing that may cause particulate formation.

The issues requested at the end of the first review cycle are as follows:

Additional compatibility testing is necessary in order to ensure that particulate is not delivered to the patient.

1. Conduct studies to identify the cause of the instability of the drug product in some admixture solutions. This should include a full chemical characterization of the particulates. ]
2. Reformulate the product so that it is compatible with admixture solutions, independent of the composition of the diluent container or administration kit.
3. As an interim solution, you may be able to market the product co-packaged with an in-line filter for removal of particulates from the admixture on administration. This will require the submission of data to demonstrate that there is no loss of potency when the admixture is filtered.

This approval provides for co-packaging with an inline filter. ]

#### **Product Labeling:**

Specific labeling comments can be found in discipline reviews. Some of the important clinical issues are highlighted below.

#### **Clinical Labeling:**

1. In the "INDICATIONS AND USAGE" section of the label:

Many physicians may incorrectly assume that the intravenous prevacid formulation is "stronger" than the oral prevacid formulation and these physicians may mistakenly believe that EE can be completely treated over the short term (in 7 days.) Therefore, the "INDICATIONS AND USAGE" section of the label should emphasize that the total recommended duration of EE treatment with prevacid is 6 to 8 weeks which includes up to 7 days of PREVACID I.V. administration.

2. In the "INDICATIONS AND USAGE" section of the label, add the statement, "The safety and efficacy of PREVACID I.V. for Injection as an initial treatment of EE have not been demonstrated."

The sponsor conducted only one PREVACID I.V. trial (Study M01-308) in EE patients. In this study, EE patients were all initially treated with oral prevacid, and then they were randomized to intravenous placebo or PREVACID I.V. Since, PREVACID I.V. has not been administered to EE patients as an initial treatment, the safety and efficacy of PREVACID I.V. in the initial treatment of EE have not been demonstrated.

3. In the “**Pediatric Use**” section of the label: include a statement that the safety and effectiveness of PREVACID I.V. for Injection have not been established for pediatric patients. Of interest is the fact that no studies have been conducted in pediatrics with this formulation. Because of its basic pH there is a concern regarding potential infusion site reactions. Future studies in pediatric patients will resolve this concern.

**CMC labeling:**

1. In the “**DOSAGE AND ADMINISTRATION**” section of the label:  
The following information is provided “PREVACID I.V. for Injection admixtures should be administered intravenously using the in-line filter provided. The filter must be used to remove precipitate that may form when the reconstituted drug product is mixed with I.V. solutions.” Currently the applicant is conducting studies regarding reformulation which when completed may provide information may allow for the removal of the filter requirement.

**PHASE IV COMMITMENTS:**

1. Conduct studies to identify the cause of the instability of the drug product in some admixture solutions. This should include a full chemical characterization of the particulates [
2. Reformulate the product so that it is compatible with admixture solutions, independent of the composition of the diluent container or administration kit.

Joyce Korvick, MD, MPH  
Deputy Division Director  
Division of Gastrointestinal and Coagulation Drug Products  
CDER/FDA

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/s/

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Joyce Korvick  
5/18/04 09:47:49 AM  
MEDICAL OFFICER

05/24/04

**Office of Drug Safety**

# Memo

**To:** Robert Justice, M.D.  
Director, Division of Gastrointestinal and Coagulation Drug Products, HFD-180

**From:** Alina R. Mahmud, R.Ph.  
Team Leader, Division of Medication Errors and Technical Support, Office of Drug Safety, HFD-420

**Through:** Carol Holquist, R.Ph.  
Director, Division of Medication Errors and Technical Support, Office of Drug Safety, HFD-420

**CC:** Melissa Furness, Project Manager, HFD-180

**Date:** May 18, 2004

**Re:** ODS Consult 03-0111-2; Prevacid I.V. (Lansoprazole for Injection); 30 mg; NDA 21-566.

---

This memorandum is in response to a May 13, 2004, request from your Division for a re-review of the proprietary name, Prevacid IV. Labels and labeling were provided for review and comment as well.

DMETS has not identified any additional proprietary or established names that have the potential for confusion with Prevacid I.V. since we conducted our review dated on August 18, 2003 (ODS consult 03-0111) that would render the name objectionable. Therefore, we have no objections to the use of this proprietary name. However, since the completion of our initial consult, the sponsor has revised the labeling and packaging of Prevacid I.V. to include an in-line filter to remove precipitate during administration. According to the Division's Project Manager, the in-line filter is temporary and the formulation will be revised so that the in-line filter will not be necessary. However, in the interim, co-packaging the drug and in-line filter may be problematic especially since post-marketing experience has shown errors with the currently marketed product, Protonix I.V. which is packaged similarly. The filter was not used in some cases and in another case, the drug was separated from the in-line filter since it required refrigeration. We recognize that Prevacid I.V. will be stored at room temperature, thus the drug and in-line filter will remain co-packaged until use. Additionally, proposed statements on labels and labeling alerting healthcare practitioners on the necessity of the in-line filter will also be helpful in preventing medication errors with the use of the in-line filter. We also recognize that upon reformulation of Prevacid I.V. the in-line will not be required. At that time, DMETS recommends that healthcare practitioners be educated on the administration of the drug product without the use of the in-line filter.

Additionally, in review of the draft labels and labeling in an attempt to focus on safety issues to prevent possible medication errors. We have identified the following areas of improvement, in the interest of minimizing user error and maximizing patient safety.

## A. GENERAL COMMENTS

1. Draft copies of the labels and labeling were provided in black and white, and may not represent the

true color of the labels and labeling. It is not possible to fully assess the safety of the labels and labeling because the information provided did not reflect the label and labeling presentation that will actually be used in the marketplace (i.e. color, placement of name, design, etc.). Please forward copies of the final printed labels and labeling when they are available.

2. It is difficult to determine the prominence of the "in-line filter required" statement on draft labels and labeling. However, we recommend that this statement appear prominently to alert pharmacists of the need to include the in-line filter when sending the product to the floors for administration. Additionally, the statement [ should be revised to read "Use of in-line filter (provided) is required" on all labels and labeling.
3. Delete the word "required" from the statement "Contains 1 single dose vial and 1 required in-line filter..." on all labels and labeling.
4. Upon reformulation and removal of in-line filter from packaging, healthcare practitioners should be educated to minimize confusion.

#### B. CARTON LABELING

Include the instructions on the "FRONT PANEL" to read, "After reconstitution with 5 mL of Sterile Water for Injection, USP, the resulting solution will contain lansoprazole 6 mg/mL (30 mg/5 mL)."

#### C. FILTER PACK LABELING

1. Revise the statement "In-line filter for use with" to read "In-line filter" and increase its prominence. Additionally, the brand name and size of the filter (PALL Supor 1.2  $\mu$ m) should appear in parenthesis immediately following the statement "In-line filter."
2. Decrease the prominence of the statement "Prevacid IV (lansoprazole) for Injection" and precede this statement with "For use with."
3. Revise the statement "Caution: Federal (USA) law restricts..." To read "Rx Only."

#### D. PEEL-OFF STICKER

Revise the statement "USE OF IN-LINE FILTER PROVIDED IS REQUIRED" to read "IN-LINE FILTER MUST BE USED."

#### E. PACKAGE INSERT

1. Provide the instructions for use to priming the filter in the DOSAGE AND ADMINISTRATION section of the Package Insert in case the labeling is lost or misplaced.
2. Increase the prominence of the statement "filter must be used to remove precipitate" which appears in the first paragraph under the heading DOSAGE AND ADMINISTRATION.

DMETS considers this a final review. However, if the approval of the NDA is delayed beyond 90 days from the date of this review, the name must be re-evaluated. A re-review of the name before NDA approval will rule out any objections based upon approvals of other proprietary/established names from this date forward. If you have any questions or need clarification, please contact Sammie Beam at 301-827-2102.

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/s/  
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Alina Mahmud  
5/25/04 03:13:23 PM  
DRUG SAFETY OFFICE REVIEWER

Carol Holquist  
5/26/04 07:39:37 AM  
DRUG SAFETY OFFICE REVIEWER



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation III

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**FACSIMILE TRANSMITTAL SHEET**

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**DATE: 05/17/04**

<b>To:</b> Nancy Knipfer, Ph.D.	<b>From:</b> Melissa Hancock Furness
<b>Company:</b> Tap Pharmaceuticals, Inc.	
<b>Fax number:</b> 847-582-2880	<b>Fax number:</b> 301-443-9285
<b>Phone number:</b> 847-582-2193	<b>Phone number:</b> 301-827-7450
<b>Subject:</b> NDA 21-566	

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**Total no. of pages including cover:** 2

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**Comments:**

We would like for you to agree to the following Post- Marketing Commitments in writing:

1. Conduct studies to identify the cause of instability of the drug product in some admixture solutions. This should include a full chemical characterization of the particulates.
2. Reformulate the product so that it is compatible with admixture solutions, independent of the composition of the diluent container or administration kit.

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/s/

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Melissa Furness  
5/17/04 04:11:06 PM  
CSO

Melissa Furness  
5/17/04 04:15:23 PM  
CSO



TAP Pharmaceutical Products Inc.  
675 North Field Drive  
Lake Forest, Illinois 60045

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## Facsimile Cover Sheet

**To:** Melissa Furness

Regulatory Health Project Manager

**Company:** FDA HFD 180

**Phone:** 301-827-7450

**Fax:** 301-443-9285

**From:** Nancianne Knipfer

Regulatory Product Manager

**Phone:** (847) 582-2193

**Fax:** (847) 582-2880

**Date:** May 17, 2004

**Pages including this**

**cover page: 5**

**RE: NDA 21-566, Phase 4 Post-approval Commitments**



TAP PHARMACEUTICAL PRODUCTS INC.

**NDA AMENDMENT**  
**Phase 4 commitments**

675 N. Field Drive  
Lake Forest, IL 60045

May 17, 2004

Robert Justice, M.D.  
Director  
Division of Gastrointestinal and Coagulation Drug Products, HFD-180  
Document Control Room 8B-45  
Center for Drug Evaluation and Research  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

**RE: PREVACID® I.V. (lansoprazole) for Injection**  
**NDA 21-566/Amendment 017**

Dear Dr. Justice,

The sponsor, TAP Pharmaceutical Products Inc. (TAP), submits this amendment to the above pending New Drug Application under the provisions of 21 CFR § 314.60. The purpose of this amendment is confirm that TAP agrees to Phase 4 post-marketing commitments as included in the FDA's Approvable letter dated October 23, 2003.

**FDA Comment:**

1. **Conduct studies to identify the cause of instability of the drug product in some admixture solutions. This should include a full chemical characterization of the particulates** [ ]).

**TAP Response:**

TAP hereby commits to conduct studies to identify the cause of instability of the drug product in some admixture solutions. This will include a full chemical characterization of the particulates [ ]

The timeframe for this commitment is [ ] after the NDA approval date.

**FDA Comment:**

2. **Reformulate the product so that it is compatible with admixture solutions, independent of the composition of the diluent container or administration kit.**

**TAP Response:**

TAP hereby commits to reformulate the product so that it is compatible with admixture solutions, independent of the composition of the diluent container or administration kit [ ] of the NDA approval date.



PREVACID® I.V. (lansoprazole) for Injection  
NDA 21-566/Amendment 017  
May 17, 2004  
Page 2 of 2

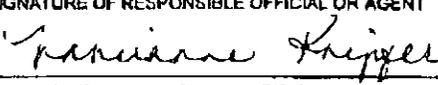
A complete and accurate filed copy has been submitted to Mr. Richard Harrison, Acting District Director of the Chicago Field Office. If you have any questions or need additional information, please contact me at the number below.

Sincerely,

A handwritten signature in cursive script that reads "Nancianne Knipfer".

Nancianne Knipfer, Ph.D.  
Regulatory Product Manager  
847-582-2193  
847-582-2880 (fax)

<b>DEPARTMENT OF HEALTH AND HUMAN SERVICES</b> <b>FOOD AND DRUG ADMINISTRATION</b>		Form Approved: OMB No. 0910-0338 Expiration Date: August 31, 2005 See OMB Statement on page 2.	
<b>APPLICATION TO MARKET A NEW DRUG, BIOLOGIC,</b> <b>OR AN ANTIBIOTIC DRUG FOR HUMAN USE</b> <i>(Title 21, Code of Federal Regulations, Parts 314 &amp; 601)</i>		<b>FOR FDA USE ONLY</b>	
		APPLICATION NUMBER	
<b>APPLICANT INFORMATION</b>			
NAME OF APPLICANT <b>TAP Pharmaceutical Products Inc.</b>		DATE OF SUBMISSION <b>5/17/04</b>	
TELEPHONE NO. (Include Area Code) <b>(847) 582-2193</b>		FACSIMILE (FAX) Number (Include Area Code) <b>(847) 582-2880</b>	
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): <b>675 North Field Drive          Lake Forest, IL 60045</b>		AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, Telephone & FAX number) IF APPLICABLE <b>Not applicable.</b>	
<b>PRODUCT DESCRIPTION</b>			
NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (if previously issued) <b>NDA 21-566</b>			
ESTABLISHED NAME (e.g., Proper name, USPIUSAN name) <b>lansoprazole</b>		PROPRIETARY NAME (trade name) IF ANY <b>PREVACID® I.V. (lansoprazole) for Injection</b>	
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (if any) <b>2[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]benzimidazole</b>		CODE NAME (if any) <b>AG-1749, A-65006</b>	
DOSAGE FORM: <b>I.V. Infusion</b>	STRENGTHS: <b>30 mg</b>	ROUTE OF ADMINISTRATION: <b>I.V.</b>	
(PROPOSED) INDICATION(S) FOR USE: <b>Short-term treatment (up to 7 days) of erosive esophagitis.</b>			
<b>APPLICATION DESCRIPTION</b>			
APPLICATION TYPE (check one) <input checked="" type="checkbox"/> NEW DRUG APPLICATION (CDA, 21 CFR 314.60) <input type="checkbox"/> ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.84) <input type="checkbox"/> BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)			
IF AN NDA, IDENTIFY THE APPROPRIATE TYPE <input checked="" type="checkbox"/> 505 (b)(1) <input type="checkbox"/> 505 (b)(2)			
IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION Name of Drug _____ Holder of Approved Application _____			
TYPE OF SUBMISSION (check one) <input type="checkbox"/> ORIGINAL APPLICATION <input checked="" type="checkbox"/> AMENDMENT TO PENDING APPLICATION <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> PRESUBMISSION <input type="checkbox"/> ANNUAL REPORT <input type="checkbox"/> ESTABLISHMENT DESCRIPTION SUPPLEMENT <input type="checkbox"/> EFFICACY SUPPLEMENT <input type="checkbox"/> LABELING SUPPLEMENT <input type="checkbox"/> CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT <input type="checkbox"/> OTHER			
IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: _____			
IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY <input type="checkbox"/> CBE <input type="checkbox"/> CBE-30 <input type="checkbox"/> Prior Approval (PA)			
REASON FOR SUBMISSION <b>Phase 4 post-marketing commitment.</b>			
PROPOSED MARKETING STATUS (check one) <input checked="" type="checkbox"/> PRESCRIPTION PRODUCT (Rx) <input type="checkbox"/> OVER THE COUNTER PRODUCT (OTC)			
NUMBER OF VOLUMES SUBMITTED <u>1</u> THIS APPLICATION IS <input checked="" type="checkbox"/> PAPER <input type="checkbox"/> PAPER AND ELECTRONIC <input type="checkbox"/> ELECTRONIC			
ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.) Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFR), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready. <b>Not applicable.</b>			
Cross References (List related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application) <b>Not applicable.</b>			

This application contains the following items: (Check all that apply)		
<input type="checkbox"/>	1. Index	
<input type="checkbox"/>	2. Labeling (check one)	<input checked="" type="checkbox"/> Draft Labeling <input type="checkbox"/> Final Printed Labeling
<input type="checkbox"/>	3. Summary (21 CFR 314.50 (c))	
<input checked="" type="checkbox"/>	4. Chemistry section	
<input checked="" type="checkbox"/>	A. Chemistry, manufacturing, and controls information (e.g., 21 CFR 314.50(d)(1); 21 CFR 601.2)	
<input type="checkbox"/>	B. Samples (21 CFR 314.50 (e)(1); 21 CFR 601.2 (e)) (Submit only upon FDA's request)	
<input type="checkbox"/>	C. Methods validation package (e.g., 21 CFR 314.50(e)(2)(i); 21 CFR 601.2)	
<input type="checkbox"/>	5. Nonclinical pharmacology and toxicology section (e.g., 21 CFR 314.50(d)(2); 21 CFR 601.2)	
<input type="checkbox"/>	6. Human pharmacokinetics and bioavailability section (e.g., 21 CFR 314.50(d)(3); 21 CFR 601.2)	
<input type="checkbox"/>	7. Clinical Microbiology (e.g., 21 CFR 314.50(d)(4))	
<input type="checkbox"/>	8. Clinical data section (e.g., 21 CFR 314.50(d)(5); 21 CFR 601.2)	
<input type="checkbox"/>	9. Safety update report (e.g., 21 CFR 314.50(d)(5)(vi)(b); 21 CFR 601.2)	
<input type="checkbox"/>	10. Statistical section (e.g., 21 CFR 314.50(d)(6); 21 CFR 601.2)	
<input type="checkbox"/>	11. Case report tabulations (e.g., 21 CFR 314.50(f)(1); 21 CFR 601.2)	
<input type="checkbox"/>	12. Case report forms (e.g., 21 CFR 314.50 (f)(2); 21 CFR 601.2)	
<input type="checkbox"/>	13. Patent information on any patent which claims the drug (21 U.S.C. 355(b) or (c))	
<input type="checkbox"/>	14. A patent certification with respect to any patent which claims the drug (21 U.S.C. 355 (b)(2) or (j)(2)(A))	
<input type="checkbox"/>	15. Establishment description (21 CFR Part 600, if applicable)	
<input type="checkbox"/>	16. Debarment certification (FD&C Act 308 (k)(1))	
<input checked="" type="checkbox"/>	17. Field copy certification (21 CFR 314.60 (l)(3))	
<input type="checkbox"/>	18. User Fee Cover Sheet (Form FDA 3387)	
<input type="checkbox"/>	19. Financial Information (21 CFR Part 54)	
<input type="checkbox"/>	20. OTHER (Specify)	
<b>CERTIFICATION</b>		
I agree to update this application with new safety information about the product that may reasonably affect the statement of contraindications, warnings, precautions, or adverse reactions in the draft labeling. I agree to submit safety update reports as provided for by regulation or as requested by FDA. If this application is approved, I agree to comply with all applicable laws and regulations that apply to approved applications, including, but not limited to the following:		
<ol style="list-style-type: none"> <li>1. Good manufacturing practice regulations in 21 CFR Parts 210, 211 or applicable regulations, Parts 606, and/or 820.</li> <li>2. Biological establishment standards in 21 CFR Part 600.</li> <li>3. Labeling regulations in 21 CFR Parts 201, 606, 610, 660, and/or 809.</li> <li>4. In the case of a prescription drug or biological product, prescription drug advertising regulations in 21 CFR Part 202.</li> <li>5. Regulations on making changes in application in FD&amp;C Act section 306A, 21 CFR 314.71, 314.72, 314.87, 314.89, and 601.12.</li> <li>6. Regulations on Reports in 21 CFR 314.80, 314.81, 600.80, and 600.81.</li> <li>7. Local, state and Federal environmental impact laws.</li> </ol>		
If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision.		
The data and information in this submission have been reviewed and, to the best of my knowledge are certified to be true and accurate.		
<b>Warning:</b> A willfully false statement is a criminal offense, U.S. Code, title 18, section 1001.		
SIGNATURE OF RESPONSIBLE OFFICIAL OR AGENT	TYPED NAME AND TITLE	DATE:
	Nancianne Knipfer, Ph.D. Regulatory Product Manager	5/17/04
ADDRESS (Street, City, State, and ZIP Code)		Telephone Number
675 North Field Drive, Lake Forest, IL 60045		( 847 ) 582-2193
Public reporting burden for this collection of information is estimated to average 24 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:		
Department of Health and Human Services Food and Drug Administration CDER, HFD-99 1401 Rockville Pike Rockville, MD 20852-1448	Food and Drug Administration CDER (HFD-94) 12229 Wilkins Avenue Rockville, MD 20852	An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-566

4-29-04

TAP Pharmaceutical Products Inc.  
Attention: Nancianne Knipfer, Ph.D.  
Product Manager, Regulatory Affairs  
675 North Field Drive  
Lake Forest, IL 60045

Dear Dr. Knipfer:

We acknowledge receipt on January 12, 2004 of your January 10, 2004 resubmission to your supplemental new drug application for Prevacid I.V. (lansoprazole) for Injection.

We consider this a complete, class 2 response to our October 23, 2003 action letter. Therefore, the user fee goal date is July 12, 2004.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have submitted pediatric studies for ages 12-17 with NDA 20-406/S-057, completed studies for ages 1-11 (NDA 20-406/S-047),  
J

If you have any questions, please call me at (301) 827-7450.

Sincerely,

*{See appended electronic signature page}*

Melissa Hancock Furness  
Regulatory Health Project Manager  
Division of Gastrointestinal and  
Coagulation Drug Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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

/s/

-----  
Melissa Furness

4/29/04 05:42:27 PM



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation III

FACSIMILE TRANSMITTAL SHEET

DATE: 04/29/04

To: Donna Kelms	From: Melissa Furness
Company: Tap Pharmaceuticals	Division of Gastrointestinal and Coagulation Drug Products
Fax number: 847-582-2880	Fax number: 301-443-9285
Phone number: 847-582-4922	Phone number: 301-827-7450
Subject: NDA 21-566	

Total no. of pages including cover: 24

Comments: <sup>find</sup>  
Please see our draft labeling recommendations. Please note that the changes were made to your proposed label submitted on 01/10/04. We look forward to discussing the attached with you from 4-5 P.M., E.S.T., on Friday, 04/30/04.

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, AND PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW.

If you are not the addressee, or a person authorized to deliver this document to the addressee, you are hereby notified that any review, disclosure, dissemination, copying, or other action based on the content of this communication is not authorized. If you have received this document in error, please notify us immediately by telephone at (301) 827-7310. Thank you.

23 Page(s) Withheld

\_\_\_\_\_ § 552(b)(4) Trade Secret / Confidential

\_\_\_\_\_ § 552(b)(5) Deliberative Process

\_\_\_\_\_ § 552(b)(5) Draft Labeling



TAP PHARMACEUTICAL PRODUCTS INC.

675 North Field Drive  
Lake Forest, IL 60045

RECEIVED

APR 30 2004

FDR/CDER

DUPLICATE

**NDA Amendment**

**Electronic Regulatory Submission  
for Archive**

April 29, 2004

BL  
ORIG AMENDMENT

Robert L. Justice, M.D., M.S., Director  
Division of Gastrointestinal and Coagulation Drug Products, HFD-180  
Parklawn Building Document Room 8B-45  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20856

**RE: NDA 21-566, Amendment No. 016  
PREVACID® I.V. (lansoprazole) for Injection  
Labeling**

Dear Dr. Justice:

The applicant, TAP Pharmaceutical Products Inc., submits this amendment to the above-listed pending new drug application under the provisions of 21 CFR 314.60.

TAP agrees with all of the recommended changes to the proposed labeling as contained in the fax of this afternoon from the Agency. The draft package insert has been revised accordingly and is enclosed in this submission. An updated version number has been assigned to the revised draft for internal tracking.

The enclosed CD-ROM includes documents in *.pdf* file format as well as the proposed labeling in *.doc* file format. All electronic files and media (~ 1 MB) provided in this submission have been scanned for computer viruses using McAfee VirusScan version 4.5.1 Service Pack 1 (Network Associates, Inc.).

Any questions or comments on this submission may be communicated to me.

Sincerely,

John R. Lieberman, Ph.D.  
Regulatory Adviser  
Phone: 847-582-5783, Fax: 847-582-2880

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION

Form Approved: OMB No. 0910-0338  
Expiration Date: August 31, 2005  
See OMB Statement on page 2.

**APPLICATION TO MARKET A NEW DRUG, BIOLOGIC,  
OR AN ANTIBIOTIC DRUG FOR HUMAN USE**  
(Title 21, Code of Federal Regulations, Parts 314 & 601)

FOR FDA USE ONLY

APPLICATION NUMBER

**APPLICANT INFORMATION**

NAME OF APPLICANT TAP Pharmaceutical Products Inc.	DATE OF SUBMISSION 4/29/04
TELEPHONE NO. (Include Area Code) (847) 582-5783	FACSIMILE (FAX) Number (Include Area Code) (847) 582-2880
APPLICANT ADDRESS (Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued): 675 North Field Drive Lake Forest, IL 60045	AUTHORIZED U.S. AGENT NAME & ADDRESS (Number, Street, City, State, ZIP Code, telephone & FAX number) IF APPLICABLE Not applicable.

**PRODUCT DESCRIPTION**

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued) NDA 21-566	
ESTABLISHED NAME (e.g., Proper name, USP/USAN name) lansoprazole	PROPRIETARY NAME (trade name) IF ANY PREVACID® I.V. (lansoprazole) for Injection
CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME (If any) 2[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl]methyl]sulfinyl]benzimidazole	CODE NAME (If any) AG-1749, A-65006
DOSAGE FORM: I.V. Infusion	STRENGTHS: 30 mg
ROUTE OF ADMINISTRATION: I.V.	

(PROPOSED) INDICATION(S) FOR USE:  
Short-term treatment (up to 7 days) of erosive esophagitis.

**APPLICATION DESCRIPTION**

APPLICATION TYPE (check one)  
 NEW DRUG APPLICATION (CDA, 21 CFR 314.50)     ABBREVIATED NEW DRUG APPLICATION (ANDA, 21 CFR 314.94)  
 BIOLOGICS LICENSE APPLICATION (BLA, 21 CFR Part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE     505 (b)(1)     505 (b)(2)

IF AN ANDA, OR 505(b)(2), IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION

Name of Drug \_\_\_\_\_ Holder of Approved Application \_\_\_\_\_

TYPE OF SUBMISSION (check one)     ORIGINAL APPLICATION     AMENDMENT TO PENDING APPLICATION     RESUBMISSION  
 PRESUBMISSION     ANNUAL REPORT     ESTABLISHMENT DESCRIPTION SUPPLEMENT     EFFICACY SUPPLEMENT  
 LABELING SUPPLEMENT     CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT     OTHER

IF A SUBMISSION OF PARTIAL APPLICATION, PROVIDE LETTER DATE OF AGREEMENT TO PARTIAL SUBMISSION: \_\_\_\_\_

IF A SUPPLEMENT, IDENTIFY THE APPROPRIATE CATEGORY     CBE     CBE-30     Prior Approval (PA)

REASON FOR SUBMISSION  
Package insert revised in accordance with the fax dated April 29, 2004 from the Agency.

PROPOSED MARKETING STATUS (check one)     PRESCRIPTION PRODUCT (Rx)     OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED 1    THIS APPLICATION IS     PAPER     PAPER AND ELECTRONIC     ELECTRONIC

ESTABLISHMENT INFORMATION (Full establishment information should be provided in the body of the Application.)  
Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

Not applicable.

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

Not applicable.

## **CONFIDENTIAL INFORMATION**

**Contains trade secret and/or confidential information which is the property of TAP PHARMACEUTICAL PRODUCTS INC. As provided by 21 CFR § 20.61, DO NOT DISCLOSE to the public.**

**1. Table of Contents for NDA 21-566 Amendment No. 016  
(n/a = not applicable)**

<b>Item Description</b>	<b>Paper archive copy volume number</b>	<b>Electronic archive copy folder</b>
Table Of Contents (Index)	1	
Labeling	1	labeling
Summary	n/a	n/a
Chemistry, Manufacturing, and Control (CMC)	n/a	n/a
NonClinical Pharmacology and Toxicology	n/a	n/a
Human Pharmacology and Bioavailability/Bioequivalence	n/a	n/a
Clinical Microbiology	n/a	n/a
Clinical	n/a	n/a
Safety Update	n/a	n/a
Case Report Tabulations (CRTs)	n/a	n/a
Case Report Forms (CRFs)	n/a	n/a
Patent Information	n/a	n/a
Patent Certification	n/a	n/a
Debarment Certification	n/a	n/a
Field Copy Certification	n/a	n/a
User Fee Cover Sheet	n/a	n/a
Financial Disclosure / Other	n/a	n/a
Other: Non-Financial	n/a	n/a

## 2. Labeling Table of Contents

Description	Review copy location volume number	Archive copy location folder/file name
Final Printed Package Insert	1	labeling\pi.pdf

Appears This Way  
On Original

28 Page(s) Withheld

\_\_\_\_\_ § 552(b)(4) Trade Secret / Confidential

\_\_\_\_\_ § 552(b)(5) Deliberative Process

\_\_\_\_\_ § 552(b)(5) Draft Labeling

**REQUEST FOR CONSULTATION**

TO (Division/Office):

**Jerry Philips, HFD-400  
Parklawn 15B-23**

FROM:

**Melissa Furness, HFD-180  
Parklawn 6B-45**

DATE  
April 21, 2004

IND NO.

NDA NO.  
21-566

TYPE OF DOCUMENT

DATE OF DOCUMENT  
January 12, 2004

NAME OF DRUG

PRIORITY CONSIDERATION

CLASSIFICATION OF DRUG

DESIRED COMPLETION DATE  
May 10, 2004

NAME OF FIRM:

**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 II MEETING | <input type="checkbox"/> FINAL PRINTED LABELING        |
| <input type="checkbox"/> NEW CORRESPONDENCE            | <input type="checkbox"/> RESUBMISSION            | <input type="checkbox"/> LABELING REVISION             |
| <input type="checkbox"/> DRUG ADVERTISING              | <input type="checkbox"/> SAFETY/EFFICACY         | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE   |
| <input type="checkbox"/> ADVERSE REACTION REPORT       | <input type="checkbox"/> PAPER NDA               | <input type="checkbox"/> FORMULATIVE REVIEW            |
| <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION | <input type="checkbox"/> CONTROL SUPPLEMENT      | <input type="checkbox"/> OTHER (SPECIFY BELOW):        |
| <input type="checkbox"/> MEETING PLANNED BY            |  |  |

**II. BIOMETRICS**

STATISTICAL EVALUATION BRANCH

STATISTICAL APPLICATION BRANCH

- |  |   |
|--|---|
| <input type="checkbox"/> TYPE A OR B NDA REVIEW  | <input type="checkbox"/> CHEMISTRY REVIEW       |
| <input type="checkbox"/> END OF PHASE II 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 IV STUDIES        | <input type="checkbox"/> IN-VIVO WAIVER REQUEST     |

**IV. DRUG EXPERIENCE**

- |  |  |
|--|--|
| <input type="checkbox"/> PHASE IV 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**

CLINICAL

PRECLINICAL

COMMENTS/SPECIAL INSTRUCTIONS:

This is a type 3 New Drug Application (2<sup>nd</sup> cycle resubmission). The PDUFA goal date is 07/12/04, but we are planning on acting on this application early, May 17, 2004. Please note that this application was submitted electronically, consequently, it may be found on the EDR (pathway - N21566/labeling folder). Also, please note that you reviewed this Tradename the first cycle and found it acceptable (ODS CONSULT #: 03-0111), but I did not know if you needed to take another look at it this cycle. Thanks much! Melissa Furness - x77450.

SIGNATURE OF REQUESTER

METHOD OF DELIVERY (Check one)

MAIL

HAND

SIGNATURE OF RECEIVER

SIGNATURE OF DELIVERER

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

-----  
Melissa Furness  
4/22/04 09:40:05 AM

## NDA/EFFICACY SUPPLEMENT ACTION PACKAGE CHECKLIST

NDA 21-566	Efficacy Supplement Type	Supplement Number
Drug: Prevacid IV		Applicant: Tap Pharmaceutical Products
RPM: Melissa Furness		HFD-180      Phone # 301-827-7450
Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)		Reference Listed Drug (NDA #, Drug name)
❖ Application Classifications:		
• Review priority		<input checked="" type="checkbox"/> Standard <input type="checkbox"/> Priority
• Chem class (NDAs only)		3
• Other (e.g., orphan, OTC)		
❖ User Fee Goal Dates		07/12/04
❖ Special programs (indicate all that apply)		<input checked="" type="checkbox"/> None <input type="checkbox"/> Subpart H <input type="checkbox"/> 21 CFR 314.510 (accelerated approval) <input type="checkbox"/> 21 CFR 314.520 (restricted distribution) <input type="checkbox"/> Fast Track <input type="checkbox"/> Rolling Review
❖ User Fee Information		
• User Fee		<input checked="" type="checkbox"/> Paid
• User Fee waiver		<input type="checkbox"/> Small business <input type="checkbox"/> Public health <input type="checkbox"/> Barrier-to-Innovation <input type="checkbox"/> Other
• User Fee exception		<input type="checkbox"/> Orphan designation <input type="checkbox"/> No-fee 505(b)(2) <input type="checkbox"/> Other
❖ Application Integrity Policy (AIP)		
• Applicant is on the AIP		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• This application is on the AIP		<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
• Exception for review (Center Director's memo)		N/A
• OC clearance for approval		N/A
❖ Debarment certification: verified that qualifying language (e.g., willingly, knowingly) was not used in certification and certifications from foreign applicants are co-signed by U.S. agent.		<input checked="" type="checkbox"/> Verified <input type="checkbox"/> N/A
❖ Patent		
• Information: Verify that patent information was submitted		<input checked="" type="checkbox"/> Verified
• Patent certification [505(b)(2) applications]: Verify type of certifications submitted		21 CFR 314.50(i)(1)(i)(A) <input type="checkbox"/> I <input type="checkbox"/> II <input type="checkbox"/> III <input type="checkbox"/> IV  21 CFR 314.50(i)(1) <input type="checkbox"/> (ii) <input type="checkbox"/> (iii) <input type="checkbox"/> Verified
• For paragraph IV certification, verify that the applicant notified the patent holder(s) of their certification that the patent(s) is invalid, unenforceable, or will not be infringed (certification of notification and documentation of receipt of notice).		<input checked="" type="checkbox"/> N/A
❖ Exclusivity Summary (approvals only)		Drafted
❖ Administrative Reviews (Project Manager, ADRA) (indicate date of each review)		02/2003

Actions	
• Proposed action	<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> AE <input type="checkbox"/> NA
• Previous actions (specify type and date for each action taken)	AE 10/23/03
• Status of advertising (approvals only)	<input checked="" type="checkbox"/> Materials requested in AP letter <input type="checkbox"/> Reviewed for Subpart H
❖ Public communications	
• Press Office notified of action (approval only)	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> Not applicable
• Indicate what types (if any) of information dissemination are anticipated	<input checked="" type="checkbox"/> None <input type="checkbox"/> Press Release <input type="checkbox"/> Talk Paper <input type="checkbox"/> Dear Health Care Professional Letter
❖ Labeling (package insert, patient package insert (if applicable), MedGuide (if applicable))	
• Division's proposed labeling (only if generated after latest applicant submission of labeling)	X
• Most recent applicant-proposed labeling	X
• Original applicant-proposed labeling	X
• Labeling reviews (including DDMAC, Office of Drug Safety trade name review, nomenclature reviews) and minutes of labeling meetings (indicate dates of reviews and meetings)	X
• Other relevant labeling (e.g., most recent 3 in class, class labeling)	N/A
Labels (immediate container & carton labels)	
• Division proposed (only if generated after latest applicant submission)	N/A
• Applicant proposed	X
• Reviews	X
❖ Post-marketing commitments	
• Agency request for post-marketing commitments	05/17/04
• Documentation of discussions and/or agreements relating to post-marketing commitments	05/17/04
❖ Outgoing correspondence (i.e., letters, E-mails, faxes)	X
❖ Memoranda and Telecons	X
❖ Minutes of Meetings	
• EOP2 meeting (indicate date)	N/A
• Pre-NDA meeting (indicate date)	N/A
• Pre-Approval Safety Conference (indicate date; approvals only)	N/A
• Other	X
❖ Advisory Committee Meeting	
• Date of Meeting	N/A
• 48-hour alert	N/A
❖ Federal Register Notices, DESI documents, NAS, NRC (if any are applicable)	N/A

Summary Reviews (e.g., Office Director, Division Director, Medical Team Leader) (indicate date for each review)	10/23/03; 10/09/03
❖ Clinical review(s) (indicate date for each review)	04/30/04; 09/30/03
❖ Microbiology (efficacy) review(s) (indicate date for each review)	04/08/03
❖ Safety Update review(s) (indicate date or location if incorporated in another review)	See Clinical Review dated 09/30/03
❖ Pediatric Page (separate page for each indication addressing status of all age groups)	Drafted
❖ Statistical review(s) (indicate date for each review)	N/A
❖ Biopharmaceutical review(s) (indicate date for each review)	02/25/04; 09/17/03
❖ Controlled Substance Staff review(s) and recommendation for scheduling (indicate date for each review)	N/A
❖ Clinical Inspection Review Summary (DSI)	
• Clinical studies	N/A
• Bioequivalence studies	N/A
<b>CMC Information</b>	
❖ CMC review(s) (indicate date for each review)	03/26/04; 10/23/03; 10/21/03; 09/29/03; 09/26/03
❖ Environmental Assessment	
• Categorical Exclusion (indicate review date)	N/A
• Review & FONSI (indicate date of review)	N/A
• Review & Environmental Impact Statement (indicate date of each review)	N/A
Micro (validation of sterilization & product sterility) review(s) (indicate date for each review)	04/08/03
❖ Facilities inspection (provide EER report)	Date completed: (X) Acceptable ( ) Withhold recommendation
❖ Methods validation	(X) Completed ( ) Requested ( ) Not yet requested
<b>Nonclinical Pharm/Tox Information</b>	
❖ Pharm/tox review(s), including referenced IND reviews (indicate date for each review)	09/15/03
❖ Nonclinical inspection review summary	N/A
❖ Statistical review(s) of carcinogenicity studies (indicate date for each review)	N/A
❖ CAC/ECAC report	N/A



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation III

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**FACSIMILE TRANSMITTAL SHEET**

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**DATE:** 12/02/03

<b>To:</b> Nancy Knipfer, Ph.D.	<b>From:</b> Melissa Hancock Furness
<b>Company:</b> Tap Pharmaceuticals, Inc.	
<b>Fax number:</b> 847-582-2880	<b>Fax number:</b> 301-443-9285
<b>Phone number:</b> 847-582-2193	<b>Phone number:</b> 301-827-7450
<b>Subject:</b> NDA 21-566/A-014 – CMC Comments	

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**Total no. of pages including cover:** 2

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**Comments:**

The proposal within the above referenced submission appears to be satisfactory. Of course, the final conclusion/decision will be based on the test data which you will be submitting to the Agency. Although the new filter that you are proposing has a similar pore size to the current one, it may contain different components/composition and/or physical properties such as burst strength. Therefore, you need to perform similar studies (particulates, potency, related substances, etc) on the new filter as well.

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/s/

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Melissa Furness  
12/2/03 10:27:53 AM  
CSO

**MEMORANDUM**

**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
PUBLIC HEALTH SERVICE  
FOOD AND DRUG ADMINISTRATION  
Center for Drug Evaluation and Research**

---

**DATE:** 10/23/03\*

**FROM:** Joyce A Korvick, MD, MPH  
DGCDP/ODE III

**SUBJECT:** Director (Deputy) Summary Approval Comments  
NDA 21-566

**APPLICANT:** TAP Pharmaceutical Products, INC.

**DRUG:** Prevacid™ (lansoprazole) Injection

**DIVISION RECOMMENDATION:**

The division has reviewed this submission and recommends that Prevacid™ (lansoprazole) Injection be made approvable pending resolution of chemistry compatibility issues. In addition the clinical reviewers recommend against including pediatric labeling for this product due to the high pH of the infused solution and the lack of actual safety data in children, specifically adverse events related to the infusion site. The label is still under negotiation and cannot be finalized until the chemistry issues are resolved.

*Appears This Way  
On Original*

### **Regulatory History:**

Prevacid is currently approved as an oral formulation for the treatment of the following: short-term treatment of active duodenal ulcer; *H. pylori* eradication to reduce the risk of duodenal ulcer recurrence; maintenance of healed duodenal ulcers; short-term treatment of active benign gastric ulcer; healing of non-steroid anti-inflammatory drugs (NSAID) associated gastric ulcer; risk reduction of NSAID- associated gastric ulcer; gastroesophageal reflux disease (GERD); short-term treatment of symptomatic GERD; short-term treatment of erosive esophagitis (EE); maintenance of healing of EE; and pathological hypersecretory conditions including Zollinger-Ellison syndrome. In addition it is labeled for use in children from age 1 year to 11 years of age.

The current application is seeking approval for the indication of the short-term treatment (up to 7 days) of all grades of erosive esophagitis as an alternative when patients are unable to take oral formulations.

Prevacid is the second drug in its class (proton pump inhibitors) to submit an application for intravenous formulation. Protonix is currently marketed in intravenous formulation with a co-packaged in-line filter.

### **Pharmacology/ Toxicology:**

The animal toxicity studies, which were submitted, had findings that were similar to those of the oral formulations. There were no new toxicity findings in the intravenous toxicity studies.

### **Biopharmaceutics:**

The major data submitted in support of this NDA came from Clinical Pharmacology studies. The applicant submitted 4 studies reporting PK and PD (acid suppression) data from crossover studies of the oral versus the IV route in healthy volunteers. According to the Biopharmaceutics review, overall, equivalent dose of 30-mg lansoprazole administered by IV 30-minute infusion every day for 7 days produces similar gastric acid output suppression compared to oral lansoprazole. "Intravenous (IV) administration of lansoprazole 30 mg QD resulted in higher systemic exposure [higher peak plasma concentration (C<sub>max</sub>) and the area under the plasma concentration-time curve (AUC) values] compared to that of oral lansoprazole 30 mg QD (C<sub>max</sub> increased by 155% and AUC increased by 35%). Intravenous 30-minute infusion of lansoprazole 30 mg QD showed an improvement over oral route in gastric acid output suppression with respect to BAO) (basal acid output), but not significantly different in terms of MAO (pentagastrin-stimulated maximum acid output) in patients on Day 7." None of these studies were performed in children.

The safety of the increased C<sub>max</sub> and AUC of the intravenous formulation will be discussed in the clinical section.

**Clinical:**

As was mentioned above, the major studies in support of this application were PK/PD. It was concluded that IV prevacid was similar in its action and efficacy to that of oral prevacid at the same dose (30-mg QD).

In support of the safety of this formulation the Integrated Summary of safety included 161 individuals who received IV lansoprazole. Sixty-two of these were patients with erosive esophagitis and the other 99 were healthy subjects. In addition to these patients Dr. Nair reviewed adverse events reported in 17 non-US trials. The analysis of these data demonstrated a safety profile that appeared comparable to that of the oral formulation regarding short-term use. The reviewer and team leader felt that based upon this data, the requested short-term dose of 30-mg QD was safe.

Finally, the currently approved oral formulations are administered in doses from 15 mg daily up to 12 weeks, to 30 mg 3 times daily for 14 days (in *H. pylori* treatment), to 60 mg daily for Zollinger-Ellison Syndrome. This provides for additional rationale on the safety of this product given the expected increased C<sub>max</sub> and AUC of the 30 mg IV compared to the 30-mg oral dose. In addition, lansoprazole has a short half-life and does not accumulate.

**Chemistry:**

The major area of concern in the CMC review of this formulation was that of compatibility. In the proposed labeling IV prevacid was to be reconstituted in 5 mL of Sterile Water for Injection, USP in preparation for use. Reconstitution yields a solution with a concentration of 6 mg/mL and a pH of approximately 11 that is stable when stored at 25°C. Before administration to the patient, further dilution in 50 mL of 0.9% Sodium chloride is required. This solution has a pH of approximately 10. Because of the small volume and length of the infusion (30 minutes) this high pH is unlikely to cause acid-base disturbances in adults. TAP states that this solution should not be mixed with other drugs or diluents due to incompatibilities. The proposed label provided for use only in 3 bags.

In a DR letter, the chemists requested the applicant perform additional compatibility studies in other bags with other diluents during this review cycle. The applicant finally did some additional testing with a second diluent (5% Dextrose) and additional bags. They included 3 bags from 3

lots of each bag. It was discovered that there was a particulate that formed in the 3 IV bags. The applicant used 3 bags. The applicant is currently performing Stage II testing of this particulate. The reason for particulate formation is as yet undetermined.

IV tubing is also used to deliver the IV formulation in addition to the bags. IV tubing is made out of a substance similar to that in the 3 bags and was not tested. Thus, while there was no apparent particulate formation in the 3 bags tested, it is not acceptable to

proceed with labeling  $\text{C}$  bag while the same solution will have to flow through tubing that may cause particulate formation.

**Conclusion:**

Additional compatibility testing is necessary in order to ensure that particulate is not delivered to the patient.

1. Conduct studies to identify the cause of the instability of the drug product in some admixture solutions. This should include a full chemical characterization of the particulates  $\text{C}$
2. Reformulate the product so that it is compatible with admixture solutions, independent of the composition of the diluent container or administration kit.
3. As an interim solution, you may be able to market the product copackaged with an in-line filter for removal of particulates from the admixture on administration. This will require the submission of data to demonstrate that there is no loss of potency when the admixture is filtered.

Joyce Korvick, MD, MPH  
Deputy Division Director  
Division of Gastrointestinal and Coagulation Drug Products  
CDER/FDA

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/s/

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Joyce Korvick  
10/23/03 04:18:59 PM  
MEDICAL OFFICER



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation III

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**FACSIMILE TRANSMITTAL SHEET**

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DATE: 10/23/03

To: Donna Helms	From: Melissa Furness
Company: TAP Pharmaceuticals	
Fax number: 847-582-2880	Fax number: [REDACTED] 301-443-9285
Phone number: 847-582-4922	Phone number: 301-827-7450
Subject: NDA 21-566 Action Letter	
Total no. of pages including cover: 4	

Comments:

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## MEMORANDUM OF TELECON

DATE: October 20, 2003

APPLICATION NUMBER: NDA 21-566, Prevacid I.V. (lansoprazole) Injection

**BETWEEN:**

Name: Donna Helms, Director, Regulatory Affairs  
Nancianne Knipfer, Ph.D., Regulatory Product Manager  
Chang Lee, M.D. M.H.A, Ph.D., Medical Director, Clinical Development  
Stephen Berge, Ph.D., Director, Pharmaceutical Development  
Dale Brinker, B.S., R.Ph., Project Leader, Pharmaceutical Development  
George Murphy, B.S., Senior Analytical Investigator  
Mary George, Ph.D., Formulation Investigator  
Janette Eichfeld, M.A., Project Manager  
Jim Tiller, PharmD, MBA, Director Health Systems  
Phone: (866) 541-8667  
Representing: TAP Pharmaceutical Products, Inc.

**AND**

Name: Susan Daugherty, Consumer Safety Officer  
Joyce Korvick, M.D., M.P.H., Deputy Division Director  
Liang Zhou, Ph.D., Chemistry Team Leader  
Ali Al-Hakim, Ph.D., Chemistry Reviewer  
Gary Della'Zanna, D.O., M.Sc., Medical Team Leader  
Representing: Division of Gastrointestinal & Coagulation Drug Products, HFD-180

SUBJECT: CMC issues regarding types of I.V. bags and diluents on particulate formation

**BACKGROUND:**

On December 23, 2002, TAP Pharmaceuticals submitted NDA 21-566 for Prevacid I.V. (lansoprazole) for Injection. A discipline review (DR) letter dated October 1, 2003, was issued that identified CMC deficiencies. Due to the potential for particulate formation with different bags and diluents, the Agency requested that the sponsor conduct compatibility studies with commonly used diluents, as well as I.V. bags of varying composition from a variety of manufacturers.

**THE CALL:**

Today, a document containing draft reports from studies conducted in response to the Agency's October 1, 2003, DR letter was faxed by the sponsor. Since the chemists have not had time to review the reports, a definitive response could not be provided at today's conference.

The draft reports demonstrated the following for Stage I testing. (Stage II testing has not been done yet.):

1. The pH did not significantly change in either the 0.9% Sodium Chloride solution or the 5% Dextrose in water solution at 0 hours, 8 hours, and 24 hours in the [ ] bag, [ ] bag, or [ ] bag.
2. All solutions and bag types that were studied passed the visual particulate test.
3. The [ ] bag failed the sub-visual particulate matter test (for particles  $\geq 10\mu\text{m}$  per container) in both the 0.9% Sodium Chloride solution and the 5% Dextrose in water solution. The [ ] bag and the [ ] bag passed this test in both the 0.9% Sodium Chloride solution and the 5% Dextrose in water solution.
4. The [ ] bag failed the sub-visual particulate matter test (for particles  $\geq 25\mu\text{m}$  per container) in the 5% Dextrose in water solution, but passed in the 0.9% Sodium Chloride solution. The [ ] bag and the [ ] bag passed this test in both the 0.9% Sodium Chloride solution and the 5% Dextrose in water solution.

The methodology for sampling requires that a different bag be used for testing each time and is kneaded prior to withdrawal of the sample.

According to the sponsor, USP Guidelines indicate that Stage II testing for particulate matter should be done for I.V. solutions that failed Stage I testing. The USP limits for amount of particulate matter in Stage II testing are lower than for Stage I (3,000 particles per container for particulate matter that is  $\geq 10\mu\text{m}$  and 300 particles per container for particulate matter that is  $\geq 25\mu\text{m}$ ).

In addition, the sponsor faxed a document containing support data for today's discussion that was previously generated. This support data tested [ ] bags with Lactated Ringer's Solution, 0.9% Sodium Chloride Solution, and 5% Dextrose in Water Solution for pH, visual inspection, and particulate matter at ambient temperature and 5°C at 0 hours and 8 hours. Only the 0.9% NaCl solution was tested at 24 hours. The data was reviewed.

The sponsor indicated that the data from analysis for degradation and potency will be available in approximately [ ]

The Agency conveyed the following concerns:

1. The action date for this application is October 23, 2003 (three days from today).
2. The site inspection is yet to be completed.
3. The chemists will need to review data submitted today in order to determine how it will effect this application.
4. Additional labeling discussions may need to occur prior to the action date, which may be difficult.
5. If today's submitted data constitutes a major amendment, we may extend the clock.
6. If an action is rendered on the goal date, the sponsor will need to agree to postmarketing commitments.

The sponsor indicated they were willing to add, [ ] to the labeling.

The Agency informed the sponsor that they would need to be prepared to provide a specific timeline, in writing, regarding the degradation and potency testing and specify why it will take a year to provide this data.

The Agency and sponsor agreed that an additional discussion would need to take place by Wednesday morning (October 22, 2003).

The call was ended.

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Joyce Korvick, M.D., M.P.H.  
Deputy Division Director

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/s/

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Susan B. Daugherty  
10/24/03 05:37:23 PM  
CSO

Joyce Korvick  
10/27/03 02:26:40 PM  
MEDICAL OFFICER  
for Dr. Robert Justice



TAP Pharmaceutical Products Inc.  
675 North Field Drive  
Lake Forest, Illinois 60045

---

## Facsimile Cover Sheet

**To:** Melissa Furness  
Dr. Joyce Korvick

**Company:** FDA  
**Phone:** (301) 827-7450  
**Fax:** (301) 443-9285

**From:** Nancianne Knipfer  
Regulatory Product Manager  
**Phone:** (847) 582-2193  
**Fax:** (847) 582-2880

**Date:** October 13, 2003

**Pages including this  
cover page:** 6

Melissa,

Attached please find a copy of cover letter for NDA 21-566/Amendment 009 for PREVACID® I.V. for Injection. Draft labeling was forwarded via email.

Please feel free to call me if you have any questions.

Sincerely,

A handwritten signature in cursive script that reads "Nancianne Knipfer".

Nancianne Knipfer, Ph.D.  
Regulatory Product Manager



TAP PHARMACEUTICAL PRODUCTS INC.

675 North Field Drive  
Lake Forest, IL 60045

**NDA Amendment**

**Chemistry, Manufacturing and Controls;  
Response to Discipline Review Letter**

**Labeling**

October 13, 2003

Robert Justice, M.D.  
Director  
Division of Gastrointestinal and Coagulation Drug Products, HFD-180  
Document Control Room 8B-45  
Center for Drug Evaluation and Research  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

**RE: PREVACID® I.V. (lansoprazole) for Injection  
NDA 21-566/Amendment 009  
Chemistry, Manufacturing and Controls; Response to Discipline Review  
Letter and Labeling**

Dear Dr. Justice,

The sponsor, TAP Pharmaceutical Products Inc. (TAP), submits this amendment to the above pending New Drug Application under the provisions of 21 CFR § 314.60. The purpose of this amendment is to respond to the Division's Discipline Review Letter dated October 1, 2003, the Division's facsimiles dated October 7 and 9, 2003 and the teleconference between the Division and TAP on October 7, 2003 for PREVACID® I.V. (lansoprazole) for Injection.

**I. DISCIPLINE REVIEW LETTER**

The Discipline Review Letter identified the following deficiencies:

**FDA Comment:**

1. **Compatibility studies should be conducted using commonly used diluents even if they are not identified in the proposed drug product labeling (e.g. Lactated Ringer's Injection, 5% Dextrose Injection, etc). The study should include:**



PREVACID® I.V. (lansoprazole) for Injection  
NDA 21-566/Amendment 009  
October 13, 2003  
Page 2 of 5

- a. **IV bags of all commercial compositions, supplied by different manufacturers, that contain various solutions.**
- b. **These studies should be performed because there is a high probability that IV bags and solutions not identified in package insert may be used in a clinical setting.**

**The studies are required because the possibility of particulate formation will result in potential potency loss and safety concerns.**

#### **TAP Response:**

Based on the communications from the Division on August 20, September 15 and September 25, 2003 and TAP responses dated August 28, September 24 and September 26, 2003, TAP planned to conduct compatibility studies and provided a timeframe C

    J This timeframe was required in order to C

    J. TAP also agreed to modifications in the labeling to highlight the type of bag and diluent studied in the I.V. stability program (Amendment 007, dated September 24, 2003). This is consistent with labeling for other I.V. products (Attachment 1).

However in the teleconference held on October 7, 2003, the Division pursued having compatibility studies completed prior to approval (Action Date, October 23, 2003). Because of reasons stated above, it was agreed that TAP would provide some limited compatibility data (i.e., bags from different suppliers and diluents of saline and dextrose [D5W]; with evaluation of foreign insoluble matter, sub-visual particulate matter and pH) prior to the Action Date, and then discuss the timeframe to provide a complete compatibility profile in various solutions and IV bags as a Phase 4 commitment.

Regarding the commercial availability of bags and diluents, it is important to remember that Prevacid I.V. is to be diluted in 50 mL of diluent (0.9 % Sodium Chloride) after the initial reconstitution of the lyophilized powder with 5 ml of Sterile Water for Injection, USP (SWFI). Based on our research, other diluents (e.g., Lactated Ringer's) are only available in bags > 50 mL. Therefore, the following combination of I.V. bags and solutions are the only 50 mL bags available for use with Prevacid I.V. (Table 1). Hospital pharmacies have access to one or more of these I.V. bags.



PREVACID® I.V. (lansoprazole) for Injection  
 NDA 21-566/Amendment 009  
 October 13, 2003  
 Page 3 of 5

**Table 1. I.V. Bags, Suppliers and I.V. Solutions Available in 50 mL Size**

I.V. Bag Material	Commercial Supplier	Solution
C		J

As agreed, TAP will perform the following test for admixtures using each of these materials:

- pH
- Foreign Insoluble Matter by Visual Inspection
- Particulate Matter – subvisual.

Testing will be performed on 3 lots of Prevacid I.V. 30 mg drug product and testing will be performed to mimic the product labeling in the following manner:

1. The vials will be reconstituted with 5 ml of SWFI and the product will be held for 1 hour prior to further dilution.
2. The reconstituted solution will be further diluted in each of the above listed bags. Testing will be performed initially and after 8 and 24 hours of holding time with one bag being tested at each interval.

TAP has scheduled the study to obtain limited compatibility information, as agreed on October 7, 2003. TAP is targeting to complete this work and to have preliminary data for review by Monday, October 20, 2003. We anticipate submitting a completed report to the Division by C J. TAP has requested a teleconference with the Division on October 20, 2003 to review these results.



PREVACID® I.V. (lansoprazole) for Injection  
NDA 21-566/Amendment 009  
October 13, 2003  
Page 4 of 5

**FDA Comment:**

2. **Three copies of methods validation should be provided. These copies should be prepared as per FDA guideline "GUIDELINE FOR SUBMITTING SAMPLES AND ANALYTICAL DATA FOR METHODS VALIDATION". Refer to 21 CFR 314.50.**

**TAP Response:**

NDA 21-566 was submitted as an electronic NDA and in accordance with guideline on electronic NDAs, a method validation package was submitted only electronically. Per your request, TAP will provide 3 paper copies of the method validation package by Friday, October 17, 2003.

**II. LABELING**

In response to the teleconference on October 7, 2003 and the Division's facsimiles dated October 7 and 9, 2003, TAP has amended the package insert, vial and carton label (Attachment 2). Per the Division's request on October 9, 2003, color copies of the vial and carton label are included in this submission (Attachment 3).

In the teleconference, a question was raised about the packaging configuration in relationship to the "J" statement.

Upon review of other I.V. product labeling, TAP has found other I.V. products, which need protection from light and are packaged in multi-unit cartons. For example, Protonix I.V. for Injection has light protection requirement, in addition to a refrigeration requirement, and is available in a carton of 5 vials. Other products include:

- Cordarone® I.V.
- TENORMIN I.V. Injection
- ZINACEF
- CLAFORAN
- Cefizox®
- Ativan® (lorazepam) Injection
- Fentanyl Citrate Injection
- ZANTAC Injection
- Norcuron®

A copy of the How Supplied section of these package inserts is provided (Attachment 4).



PREVACID® I.V. (lansoprazole) for Injection  
NDA 21-566/Amendment 009  
October 13, 2003  
Page 5 of 5

In addition, we found that several of these package inserts provide instructions to store the product in the carton in order to protect from light. Therefore, in consideration of your concern, we are adding the following statement to the package insert and carton:

[

].

Finally, it is acceptable pharmacy practice to store products as recommended in the labeling and as recommended in the guideline issued by the American Society of Health Systems Pharmacists entitled, "*ASHP Guidelines on Quality Assurance for Pharmacy-Prepared Sterile Products*" (Attachment 5). The guideline states the following:

"Warehouse and other pharmacy storage areas where ingredients are stored should be monitored to ensure that temperature, *light*, moisture, and ventilation remain within manufacturer and compendial requirements."

The Joint Commission on Accreditation of Healthcare Organizations recognizes this guideline during their accreditation process.

A complete and accurate copy of this submission has been submitted to the District Director of the Chicago Field Office.

Please direct any questions or comments concerning this submission to my attention.

Sincerely,

A handwritten signature in cursive script that reads 'Nancianne Knipfer'.

Nancianne Knipfer, Ph.D.  
Regulatory Product Manager  
847-582-2193  
847-582-2880 (fax)

Attachments

CC: Dr. Joyce Korvick, Deputy Director, DGCDP  
Melissa Furness, Consumer Safety Officer

**Furness, Melissa**

---

**From:** nancianne.knipfer@TAP.com  
**Sent:** Tuesday, October 21, 2003 12:50 PM  
**To:** furnessm@cder.fda.gov  
**Subject:** PREVACID IV Labeling for submission

Melissa,

I have just faxed you amendment 11, which contains our phase 4 commitment and revised labeling. I have attached electronic copies for your convenience.

**Timeline for Phase 4 commitment**

Nancianne Knipfer, Ph.D.  
Regulatory Product Manager  
TAP Pharmaceutical Product Inc.  
675 North Field Drive  
Lake Forest, IL 60045  
Tel: 847-582-2193  
Cell: 773-531-7300  
Fax: 847-582-2880

54 Page(s) Withheld

\_\_\_\_\_ § 552(b)(4) Trade Secret / Confidential

\_\_\_\_\_ § 552(b)(5) Deliberative Process

\_\_\_\_\_ § 552(b)(5) Draft Labeling



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation III

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**DATE: 10/09/03**

<b>To: Nancy Knipfer, Ph.D.</b>	<b>From: Melissa Hancock Furness</b>
<b>Company: Tap Pharmaceuticals, Inc.</b>	
<b>Fax number: 847-236-2880</b>	<b>Fax number: 301-443-9285</b>
<b>Phone number: 847-236-2193</b>	<b>Phone number: 301-827-7450</b>
<b>Subject: NDA 21-566 – Labeling Comments</b>	

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The Agency has the following additional comments regarding your proposed label for NDA 21-566:

A. GENERAL COMMENTS (Prevacid I.V. 30 mg)

1. Please forward color copies of the final printed labels and labeling when they are available.
2. Include the product strength "30 mg" prominently displayed under the established name. For example: "30 mg/vial".

B. CONTAINER LABELS (Prevacid I.V. 30 mg Single Dose Vial)

1. Add the statement "For I.V. infusion only." to the principal display (front) panel. Additionally, the statement "Must be further diluted before I.V. use." should appear in conjunction with this statement.
2. Revise the instructions on "SIDE PANEL B" to read, "After reconstitution with 5 mL of Sterile Water for Injection, USP, the resulting solution will contain lansoprazole 6 mg/mL (30 mg/5 mL)."
3. Move "Contains: 30 mg of lansoprazole" to a side panel and revise to read, "Each vial contains 30 mg of lansoprazole."
4. If possible, increase the prominence of "Do not administer with other intravenous solutions or drugs." on Side Panel B.
5. List the inactive ingredients on a side panel of the label.

C. CARTON LABELING (Prevacid I.V. 30 mg – 10 Single Dose Vials)

Revise the instructions on the "FRONT PANEL" to read, "After reconstitution with 5 mL of Sterile Water for Injection, USP, the resulting solution will contain lansoprazole 6 mg/mL (30 mg/5 mL)."

D. INSERT LABELING (Prevacid I.V. 30 mg)

1. DOSAGE AND ADMINISTRATION

Revise the instructions to read, "After reconstitution with 5 mL of Sterile Water for Injection, USP, the resulting solution will contain lansoprazole 6 mg/mL (30 mg/5 mL). Mix gently until the powder is dissolved."

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/s/

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Melissa Furness  
10/9/03 03:57:39 PM  
CSO



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation III

FACSIMILE TRANSMITTAL SHEET

DATE: 10/07/03

To: Nanci Kripter	From: Melissa Furness
Company: TAP Pharmaceuticals	
Fax number: 847-582-2880	Fax number: 301-443-9285
Phone number: 847-582-2193	Phone number: 301-827-7450
Subject: NDA 21-566	

Total no. of pages including cover. 23

Comments: Please find our early draft recommendations. Please note that these changes were not made to your label submitted on 09/24/03. We look forward to discussing the attached with you from 4-5 PM, EST, today.

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22 Page(s) Withheld

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\_\_\_\_\_ § 552(b)(5) Deliberative Process

\_\_\_\_\_ § 552(b)(5) Draft Labeling



NDA 21-566

**DISCIPLINE REVIEW LETTER**

16-1-03

TAP Pharmaceutical Products Inc.  
Attention: Nancianne Knipfer, Ph.D.  
Project Manager, Regulatory Affairs  
675 North Field Drive  
Lake Forest, IL 60045

Dear Dr. Knipfer:

Please refer to your December 20, 2002 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prevacid IV (lansoprazole).

We also refer to your submissions dated April 21, August 12, August 28, September 4, September 8, September 24, and September 26, 2003.

Our review of the Chemistry, Manufacturing and controls section of your submission is complete, and we have identified the following deficiencies:

1. Compatibility studies should be conducted using commonly used diluents even if they are not identified in the proposed drug product labeling (e.g. Lactated Ringer's Injection, 5% Dextrose Injection, etc). The study should include:
  - a) IV bags of all commercial compositions, supplied by different manufacturers, that contain various solutions
  - b) These studies should be performed because there is a high probability that IV bags and solutions not identified in package insert may be used in a clinical setting.

The studies are required because the possibility of particulate formation will result in potential potency loss and safety concerns.

2. Three copies of methods validation should be provided. These copies should be prepared as per FDA guideline "GUIDELINE FOR SUBMITTING SAMPLES AND ANALYTICAL DATA FOR METHODS VALIDATION". Refer to 21 CFR 314.50.

We are providing these comments to you before we complete our review of the entire application to give you preliminary notice of issues that we have identified. In conformance with the prescription drug user fee reauthorization agreements, these comments do not reflect a final

NDA 21-566

Page 2

decision on the information reviewed and should not be construed to do so. These comments are preliminary and subject to change as we finalize our review of your application. In addition, we may identify other information that must be provided before we can approve this application. If you respond to these issues during this review cycle, depending on the timing of your response, and in conformance with the user fee reauthorization agreements, we may not be able to consider your response before we take an action on your application during this review cycle.

If you have any questions, call Melissa Hancock Furness, Regulatory Project Manager, at (301) 827-7450.

Sincerely,

Liang Zhou, Ph.D.  
Chemistry Team Leader for the  
Division of Gastrointestinal & Coagulation Drug  
Products, HFD-180  
DNDC DNDC II, Office of New Drug Chemistry  
Center for Drug Evaluation and Research

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/s/

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Liang Zhou  
10/1/03 03:58:17 PM



Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation III

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**FACSIMILE TRANSMITTAL SHEET**

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**DATE:** 09/25/03

<b>To:</b> Nancy Knipfer, Ph.D.	<b>From:</b> Melissa Hancock Furness
<b>Company:</b> Tap Pharmaceuticals, Inc.	
<b>Fax number:</b> 847-236-2880	<b>Fax number:</b> 301-443-9285
<b>Phone number:</b> 847-236-2193	<b>Phone number:</b> 301-827-7450
<b>Subject:</b> NDA 21-566 – CMC Comments	

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**Total no. of pages including cover:** 2

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**Comments:**

In addition to assessing the compatibility of drug products admixed with diluents identified in the labeling, compatibility studies should also be performed with commonly used diluents even if they are not identified in the drug product labeling. These studies should be performed because it is likely that the diluents will be used whether or not they are specifically discussed in labeling. At a minimum, admixing with Lactated Ringer's Injection, 5% weight/volume (w/v) Dextrose Injection, etc.

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Melissa Furness  
9/25/03 09:47:57 AM  
CSO

**NDA Amendment  
Chemistry, Manufacturing and  
Controls & Labeling**

**Electronic Media for Archive**

September 24, 2003

Robert Justice, M.D.  
Director  
Division of Gastrointestinal and Coagulation Drug Products, HFD-180  
Document Control Room 8B-45  
Center for Drug Evaluation and Research  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

**RE: PREVACID® I.V. (lansoprazole) for Injection  
NDA 21-566/Amendment 007  
Chemistry, Manufacturing and Controls & Labeling**

Dear Dr. Justice,

The sponsor, TAP Pharmaceutical Products Inc. (TAP), submits this amendment to the above pending New Drug Application under the provisions of 21 CFR § 314.60. The purpose of this amendment is to respond to the Agency's facsimile dated September 15, 2003 for PREVACID I.V. (lansoprazole) for Injection.

**FDA Comment:**

**Your amendment to the above mentioned NDA, dated August 28, 2003, indicated that Tap agrees to conduct additional compatibility studies with other commonly used I.V. bags. Please let us know when the results of these studies are going to be submitted to the NDA.**

**TAP Response:**

TAP agrees to conduct additional compatibility studies with other commonly used I.V. bags and to submit the results to the NDA          7. of the NDA approval.

PREVACID® I.V. (lansoprazole) for Injection  
NDA 21-566/Amendment 007  
September 24, 2003  
Page 2 of 2

As indicated in NDA 21-566/A-004, dated August 28, 2003, TAP agreed to amend the labeling to indicate that I.V. bags  should be used. The revised package insert, carton and vial label are included in this submission.

The enclosed CD-ROM includes documents in *.pdf* file format as well as the proposed labeling in *.doc* file format. All electronic files and media (~ 1 MB) provided in this submission have been scanned for computer viruses using McAfee VirusScan version 4.5.0.534 (Network Associates, Inc.).

A complete and accurate copy of this submission has been submitted to Mr. Arlyn H. Baumgarten, District Director of the Chicago Field Office.

Attached is Form FDA 356h to complete this submission. Please direct any questions or comments concerning this submission to my attention.

Sincerely,

Nancianne Knipfer, Ph.D.  
Regulatory Product Manager  
847-582-2193  
847-582-2880 (fax)

Attachments

25 Page(s) Withheld

\_\_\_\_\_ § 552(b)(4) Trade Secret / Confidential

\_\_\_\_\_ § 552(b)(5) Deliberative Process

\_\_\_\_\_ § 552(b)(5) Draft Labeling

9 Page(s) Withheld

\_\_\_\_\_ § 552(b)(4) Trade Secret / Confidential

\_\_\_\_\_ § 552(b)(5) Deliberative Process

\_\_\_\_\_ § 552(b)(5) Draft Labeling



**Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Drug Evaluation III**

**FACSIMILE TRANSMITTAL SHEET**

**DATE:** August 20, 2003

<b>To:</b> Nanciane Knipfer, Ph.D. Regulatory Product Manager	<b>From:</b> Alice Kacuba, R.N., MSN, RAC Regulatory Health Project Manager
<b>Company:</b> TAP Pharmaceutical Products Inc.	Division of Gastrointestinal and Coagulation Drug Products
<b>Fax number:</b> 847-236-2880	<b>Fax number:</b> 301-443-9285
<b>Phone number:</b> 847-236-2193	<b>Phone number:</b> (301) 827-1602 or 7310
<b>Subject:</b> <del>NDA 21-566</del>	

**Total no. of pages including cover:** \_\_\_\_\_

**Comments:** CMC Information Requests. Please note that the cmc review is still in progress but these are the Information Requests that we have to date. There may be additional requests as the review progresses.

**Documents to be mailed:**      •• YES                       NO

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Chemistry Information Requests:

1. Provide information to support your conclusion that [redacted] as stated in the NDA.
2. Please repeat your container compatibility studies using other IV bags [redacted] which are commercially available and may be used to deliver the lansoprazole IV solution.
3. Related substances specifications need to be revised and tightened based on test data obtained from your long-term stability study taking into consideration the threshold allowed in the ICH guideline (Q3B). [redacted]
4. Provide CMC information (preparation, characterization, storage, testing, etc.) regarding the drug product reference standards.
5. According to NDA, the drug substance [redacted]  
Please explain. [redacted]
6. Provide information regarding the [redacted] plan used in the drug product testing using the proposed analytical methods.

Additional comments:

1. Please be aware that [redacted] is more than the amount allowed by USP for recommended excess volume for injection [redacted]
2. The recommended expiration dating for the drug product will be based on satisfactory real time stability data and not extrapolation of the data; however, an additional 6 months may be granted depending on the quality of the stability data.

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/s/

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Alice Kacuba  
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**FACSIMILE TRANSMITTAL SHEET**

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**DATE:** 09/15/03

<b>To:</b> Nancy Knipfer, Ph.D.	<b>From:</b> Melissa Hancock Furness
<b>Company:</b> Tap Pharmaceuticals, Inc.	
<b>Fax number:</b> 847-236-2880	<b>Fax number:</b> 301-443-9285
<b>Phone number:</b> 847-236-2193	<b>Phone number:</b> 301-827-7450
<b>Subject:</b> NDA 21-566	

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**Total no. of pages including cover:** 2

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**Comments:**

Your amendment to the above mentioned NDA, dated August 28, 2003, indicated that Tap agrees to conduct additional compatibility studies with other commonly used I.V. bags. Please let us know when the results of these studies are going to be submitted to the NDA.

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/s/

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Melissa Furness .  
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CSO

09/09/03

**CONSULTATION RESPONSE**

**Division of Medication Errors and Technical Support  
Office of Drug Safety  
(DMETS; HFD-420)**

**DATE RECEIVED:** MAR-24-2003

**DESIRED COMPLETION DATE:** MAY-24-2003  
**PDUFA DATE:** OCT-23-2003

**ODS CONSULT #:**  
03-0111

**TO:** Robert Justice, MD  
Director, Division of Gastrointestinal and Coagulation Drug Products  
HFD-180

**THROUGH:** Melissa Furness  
Project Manager, Division of Gastrointestinal and Coagulation Drug Products  
HFD-180

**PRODUCT NAME:**  
Prevacid I.V.  
(Lansoprazole for Injection)  
30 mg

**NDA SPONSOR:**  
Tap Pharmaceuticals Inc.

**NDA #** 21-566

**SAFETY EVALUATOR:** Marci Lee, PharmD

**SUMMARY:** In response to a consult from the Division of Gastrointestinal and Coagulation Drug Products (HFD-180), the Division of Medication Errors and Technical Support (DMETS) conducted a review of the proposed proprietary name, "Prevacid I.V.", to determine the potential for confusion with approved proprietary and established names as well as pending names.

**RECOMMENDATIONS:**

1. DMETS has no objections to the use of the proprietary name, Prevacid I.V.
2. DMETS recommends the labeling revisions outlined in Section III to promote the safest possible use of this product.
3. DDMAC finds the proprietary name, Prevacid I.V., acceptable from a promotional perspective.

\_\_\_\_\_  
Carol Holquist, RPh  
Deputy Director  
Division of Medication Errors and Technical Support  
Office of Drug Safety  
Phone: (301) 827-3242 Fax (301) 443-9664

\_\_\_\_\_  
Jerry Phillips, RPh  
Associate Director  
Office of Drug Safety  
Center for Drug Evaluation and Research  
Food and Drug Administration

**Division of Medication Errors and Technical Support  
Office of Drug Safety  
HFD-420; Parklawn Building Room 6-34  
Center for Drug Evaluation and Research**

**PROPRIETARY NAME REVIEW**

**DATE OF REVIEW:** August 18, 2003  
**NDA NUMBER:** 21-566  
**NAME OF DRUG:** Prevacid I.V. (Lansoprazole for Injection) 30 mg  
**NDA SPONSOR:** Tap Pharmaceuticals Inc.

**I. INTRODUCTION**

This consult was written in response to a request from the Division of Gastrointestinal and Coagulation Drug Products (HFD-180) for an assessment of the proposed proprietary name, Prevacid I.V. The draft container labels, carton and package insert labeling were reviewed for possible interventions in minimizing medication errors.

The sponsor is currently marketing Prevacid as a delayed-release oral capsule, oral tablet (disintegrating), and extended-release oral suspension. These formulations were approved May 10, 1995, August 30, 2002 and May 3, 2001, respectively.

**PRODUCT INFORMATION**

Prevacid I.V. is the proposed name for Lansoprazole for Injection. Prevacid I.V. is indicated as an alternative for the short-term treatment (up to seven days) of all grades of erosive esophagitis. Once the patient is able to take medications orally, therapy can be switched to either Prevacid delayed-release capsules, Prevacid for delayed-release oral suspension, or Prevacid SoluTab Delayed Release orally disintegrating tablets.

The recommended adult dose is 30 mg lansoprazole per day administered by intravenous infusion over 30 minutes for up to 7 days. No dosage adjustment is necessary in patients with renal insufficiency or the elderly. For patients with severe liver disease, dosage adjustment should be considered.

The safety and effectiveness of Prevacid have been established for pediatric patients, in the age group of one year to 11 years, for short-term, oral treatment of symptomatic gastroesophageal reflux disease (GERD) and erosive esophagitis. Doses for the pediatric patient population range from 15 mg to 30 mg daily.

Prevacid I.V. will be available as a lyophilized powder containing 30 mg of lansoprazole per vial. Cartons of Prevacid I.V. will contain 10 vials.

## II. RISK ASSESSMENT

The medication error staff of DMETS conducted a search of several standard published drug product reference texts<sup>1,2</sup> as well as several FDA databases<sup>3</sup> for existing drug names which sound-alike or look-alike to "Prevacid I.V." 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 trademark electronic search system (TESS) was conducted<sup>4</sup>. The Saegis<sup>5</sup> 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 prescription analysis studies, involving health care practitioners within FDA. These exercises were conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the names.

### A. EXPERT PANEL DISCUSSION

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name, Prevacid I.V. Potential concerns regarding drug marketing and promotion related to the proposed names 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. DDMAC did not have concerns about the name with regard to promotional claims.
2. The Expert Panel identified potential for confusion with Primaxin and Primacor. The product information is listed in Table 1 (See below on page 3), including the dosage forms available and usual dosage.

Table 1. Potential Sound-Alike and/or Look-Alike Names Identified by DMETS Expert Panel

Product Name	Established name, Dosage form(s)	Usual adult dose	Look-alike or Sound-alike
Prevacid I.V.	Lansoprazole for Injection 30 mg vial	30 mg I.V. daily for up to seven days	
Primaxin I.V.	Imipenem and Cilastatin 250 mg/250 mg 500 mg/500 mg 750 mg/750 mg (Primaxin I.M.)	I.V.: 250 mg to 500 mg every 6 or 8 hours IM: 500 mg to 750 mg every 12 hours	Look-alike
Primacor	Milrinone Lactate 1 mg/mL in 10 mL, 20 mL, 50 mL Single dose vials 200 mcg/mL premix 100 mL	Load with 50 mcg/kg Maintenance dose is individualized but standard is 0.5 mcg/kg/min	Look-alike

\*Frequently used, not all-inclusive.

<sup>1</sup> MICROMEDEX Integrated Index, 2003, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

<sup>2</sup> Facts and Comparisons, 2003, Facts and Comparisons, St. Louis, MO.

<sup>3</sup> The DMETS database of proprietary name consultation requests, New Drug Approvals 98-03, and the electronic online version of the FDA Orange Book.

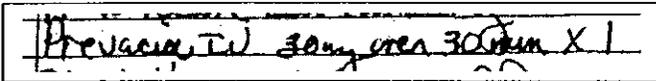
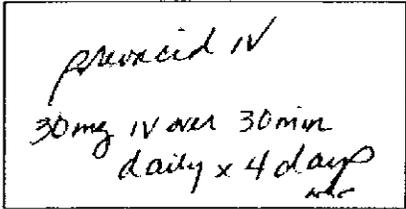
<sup>4</sup> WWW location <http://www.uspto.gov/main/trademarks.htm>

<sup>5</sup> Data provided by Thomson & Thomson's SAEGIS(tm) Online Service, available at [www.thomson-thomson.com](http://www.thomson-thomson.com).

## B. PRESCRIPTION ANALYSIS STUDIES

### 1. Methodology

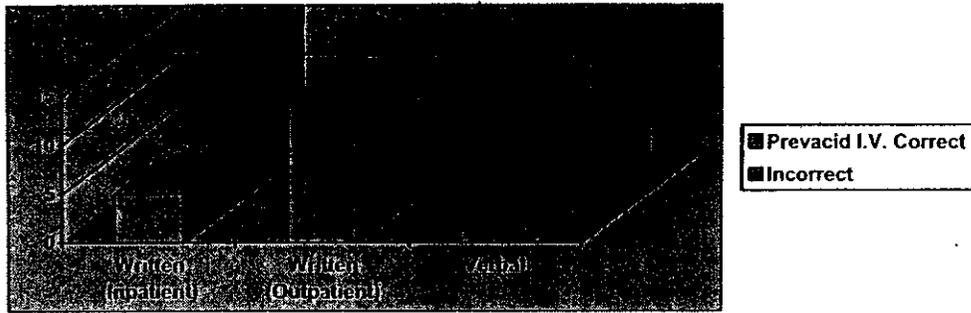
Three separate studies were conducted within FDA for the proposed proprietary name to determine the degree of confusion of Prevacid I.V. with other U.S. drug names due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 105 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Prevacid I.V. (See below). These prescriptions were optically scanned and one prescription was delivered to each of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to each of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTIONS		VERBAL PRESCRIPTION
Prevacid I.V.		
Inpatient:		
Outpatient:		Verbal: "...the third prescription is for Prevacid I.V. Use as directed over four days. Number four."

### 2. Results

Table 2. Results of these exercises are summarized below:

Study	# of Participants	# of Responses	"Prevacid I.V." Response	Other Response
Written: Inpatient	39	20 (51%)	5 (25%)	15 (75%)
Written Outpatient	35	19 (54%)	14 (74%)	5 (26%)
Verbal:	31	17 (55%)	14 (82%)	3 (18%)
Total:	105	56 (53%)	33 (59%)	23 (41%)



Among participants in the written prescription studies, 20 of 74 respondents (27%) interpreted the name incorrectly. However, several of the "incorrect" responses were partially correct. Eleven of the incorrect responses were *Prevacid*, omitting the "I.V." modifier. Additionally, two incorrect responses were *Prevacid Intravenous*, providing the interpretation of the "I.V." modifier in the response.

Other incorrect interpretations included: *Prevacia I.V.* (2 occurrences), *Prevacia* (1 occurrence), *Prevacin* (1 occurrence), *Prevacin I.V.* (1 occurrence), *Prevacine I.V.* (1 occurrence), and *Prevacor I.V.* (1 occurrence). None of the interpretations are similar to a currently marketed drug product.

Among participants in the verbal prescription studies, 3 of 17 (18%) interpreted the name incorrectly. However, all of the incorrect responses were phonetically equivalent to *Prevacid I.V.* These included *Pravacid* (1 occurrence) and *Previdid I.V.* (2 occurrences).

#### C. ADVERSE EVENT REPORTING SYSTEM (AERS)

*Prevacid* has been marketed since May 1995, therefore DMETS conducted a search of the FDA Adverse Event Reporting System (AERS). This search yielded 11 medication error reports involving, *Prevacid* or lansoprazole. Of the 11 reports, four of them involved drug name confusion. These four reports are summarized in Appendix A.

Two reports describe potential for confusion between *Prevacid* and *Pravachol*. The other reports describe confusion with the established names aripiprazole and lansoprazole. Aripiprazole is an antipsychotic, while lansoprazole is a proton pump inhibitor.

#### D. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name, *Prevacid I.V.*, the primary concerns raised were related to *Primaxin* and *Primacor*, which already exist in the U.S. marketplace. Additionally, a search of the medication error reports for *Prevacid* in AERS identified potential for look-alike confusion with *Pravachol*.

##### 1. Review of the proprietary name, *Prevacid I.V.*

- a. *Primaxin* has potential for look-alike confusion with *Prevacid I.V.* When handwritten, the letters "Prima-" and "Preva-" look similar. Also, two of the responses to the written prescription studies indicated that the "-cid" ending looked like "-cin", which is similar to "-xin". Depending upon the height of the

handwritten letter "d", the endings "-xin" and "-cid" may actually help to differentiate the names. Primaxin is an antibiotic indicated to treat serious infections. Some institutions restrict the use of Primaxin or require approval by their Infectious Diseases department prior to dispensing. This restriction minimizes the likelihood for errors with Prevacid to reach patients in those settings. Unlike Prevacid, Primaxin contains a combination of two active ingredients. Additionally, there is no overlap in dosage strength or dosing schedule. Prevacid I.V. and Primaxin could be stored near one another on a pharmacy shelf before the doses are prepared or after reconstitution and dilution in a patient care area. However, DMETS anticipates that Prevacid I.V. and Primaxin I.V. will coexist safely due to the product differences. In addition, the Prevacid name has been on the market since May 10, 1995. This helps to minimize the likelihood for confusion with Primaxin because the Prevacid name has gained familiarity among practitioners. At this time, DMETS is not aware of an medication error reports that describe confusion between Prevacid and Primaxin.

*Prevacid I.V. Primaxin I.V.*

- b. Primacor has potential for look-alike confusion with Prevacid I.V. The look-alike similarity is mainly due to the beginning letters, "Preva-" and "Prima-". Although one respondent to the written prescription study saw "Prevacor I.V.", the endings "-cor" and "-cid" can actually help to differentiate the names when handwritten. Again this depends on the height of the handwritten letter "d". Primacor is a short term I.V. therapy indicated to treat congestive heart failure. Primacor is administered as a continuous intravenous infusion that is adjusted according to the patient's response to the therapy. This also means that the patients receiving Primacor require special monitoring. There is no overlap of the dosing instructions or dosage strengths for Prevacid I.V. and Primacor. It is possible that these products could be stored near one another on a pharmacy shelf. Both products are available as a 10 mL single dose vial. However, DMETS anticipates that Prevacid I.V. and Primacor will coexist safely due to the differences of these products.

*Prevacid I.V. Primacor I.V.*

2. Concern with "I.V." portion of Prevacid I.V.

The Expert Panel identified additional concerns regarding the "I.V." portion of the proposed name. One concern was the potential for "I.V." to be misinterpreted in this context as the Roman numeral four. Another concern was the potential for Prevacid I.V. to be administered as an intramuscular injection, in error.

However, an AERS search for medication errors associated with "I.V." in the proprietary name yielded no relevant reports of this type of confusion.

### 3. Name Confusion identified in AERS search results

Pravachol was identified to have potential for look-alike confusion with Prevacid in two medication error reports from 1997 and 1999. Again, the look-alike similarity is mainly due to the similar beginning letters, "Prava-" and "Preva-". Additionally, the ending letters "-l" and "-d" can look alike. The handwriting sample below was submitted with one report. Pravachol is indicated for treatment of hypercholesterolemia. DMETS anticipates that the existence of an intravenous formulation of Prevacid is not likely to increase the risk for confusion between Pravachol and Prevacid. Finally, the "I.V." portion of Prevacid I.V. can further help to differentiate the names.

## III. LABELING, PACKAGING AND SAFETY RELATED ISSUES

DMETS has reviewed the draft container label, carton labeling and package insert labeling in an attempt to focus on safety issues to prevent possible medication errors. We have identified the following areas of improvement, in the interest of minimizing user error and maximizing patient safety.

### A. GENERAL COMMENTS (Prevacid I.V. 30 mg)

1. Draft copies of the labels and labeling were provided in black and white, and may not represent the true color of the labels and labeling. It is not possible to fully assess the safety of the labels and labeling because the information provided did not reflect the label and labeling presentation that will actually be used in the marketplace (i.e. color, placement of name, design, etc.). Please forward copies of the final printed labels and labeling when they are available.
2. Include the product strength "30 mg" prominently displayed under the established name. For example: "30 mg/vial".

### B. CONTAINER LABELS (Prevacid I.V. 30 mg Single Dose Vial)

1. Add the statement "For I.V. infusion only." to the principal display (front) panel. Additionally, the statement "Must be further diluted before I.V. use." should appear in conjunction with this statement.
2. Revise the instructions on "SIDE PANEL B" to read, "After reconstitution with 5 mL of Sterile Water for Injection, USP, the resulting solution will contain lansoprazole 6 mg/mL (30 mg/5 mL)."
3. Move "Contains: 30 mg of lansoprazole" to a side panel and revise to read, "Each vial contains 30 mg of lansoprazole."
4. If possible, increase the prominence of "Do not administer with other intravenous solutions or drugs." on Side Panel B.
5. List the inactive ingredients on a side panel of the label.

C. **CARTON LABELING (Prevacid I.V. 30 mg – 10 Single Dose Vials)**

Revise the instructions on the "FRONT PANEL" to read, "After reconstitution with 5 mL of Sterile Water for Injection, USP, the resulting solution will contain lansoprazole 6 mg/mL (30 mg/5 mL)."

D. **INSERT LABELING (Prevacid I.V. 30 mg)**

1. **DOSAGE AND ADMINISTRATION**

Revise the instructions to read, "After reconstitution with 5 mL of Sterile Water for Injection, USP, the resulting solution will contain lansoprazole 6 mg/mL (30 mg/5 mL). Mix gently until the powder is dissolved."

**IV. RECOMMENDATIONS**

1. DMETS has no objection to the use of the proprietary name, Prevacid I.V.
2. DMETS recommends the labeling revisions outlined in Section III to promote the safest possible use of this product.
3. DDMAC finds the proprietary name, Prevacid I.V., acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this consult. We are willing to meet with the Division for further discussion as well. If you have any questions concerning this review, please contact Sammie Beam at 301-827-3242.

---

Marci Lee, PharmD  
Safety Evaluator  
Office of Drug Safety (DMETS)

Concur:

---

Denise Toyer, PharmD  
Team Leader  
Division of Medication Errors and Technical Support  
Office of Drug Safety

## APPENDIX A – Prevacid Medication Error Reports

1. ISR # 3243756-6/Date Received by FDA APR-22-1999  
Potential error report  
Event date unknown  
[ ]  
Illegible and incomplete order.

“See file for copy of an illegible and incomplete order for ‘Prevacid or Pravachol’ which could potentially cause a potential medication error or delay in therapy.”

Prevacid Prevacid? Pravachol?

2. ISR # 3243756-6/Date Received by FDA JUL-28-2003  
Potential error report  
Report date JUN-23-1997  
Unknown location

“A pharmacist reported that there is a potential to confuse **Prevacid** or **Pravachol**.”

3. ISR # 4072218-1/Date Received by FDA MAR-12-2003  
Potential error report  
Event date unknown  
< >  
Generic name suffix confusion.

“New atypical anti-psychotic on the market Abilify (aripiprazole). The generic name has a suffix that looks, spells and sounds like a proton pump inhibitor (omeprazole, lansoprazole, etc.). Further, the dose of aripiprazole is similar to the PPI’s (10 mg, 15 mg, 20 mg). A poorly phrased or enunciated verbal order may cause confusion, especially if the recipient of the order is unfamiliar with this new drug.”

4. ISR # 4082803-9/Date Received by FDA MAR-27-2003  
Actual error report  
Event date unknown  
( )  
Medication did not reach patient.

“A physician at our institution (a community hospital) recently ordered Abilify 15 mg daily for a patient. A new pharmacist came to question if this drug could be automatically therapeutically interchanged for lansoprazole, our PPI of choice. He apparently had seen that the generic name of Abilify is aripiprazole, and had assumed that the drug was a new PPI because of the –prazole ending. The fact that Abilify dosing is 10 – 15 mg daily is also similar to dosing for a PPI.”

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/s/

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Marci Ann Lee  
9/9/03 09:09:07 AM  
DRUG SAFETY OFFICE REVIEWER

Carol Holquist  
9/9/03 11:06:04 AM  
DRUG SAFETY OFFICE REVIEWER

Jerry Phillips  
9/9/03 11:36:03 AM  
DRUG SAFETY OFFICE REVIEWER



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/s/

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Melissa Furness  
9/3/03 03:36:57 PM  
CSO

**Electronic Media for Archive**

**NDA Amendment  
Chemistry, Manufacturing, and  
Controls, Labeling, & Other  
(Pediatric Development Plan)**

■ April 21, 2003

Robert Justice, M.D.  
Director  
Division of Gastrointestinal and Coagulation Drug Products, HFD-180  
Document Control Room 8B-45  
Center for Drug Evaluation and Research  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

**RE: PREVACID® I.V. (lansoprazole) for Injection  
NDA 21-566/Amendment 002  
Chemistry, Manufacturing and Controls, Labeling, & Other (Pediatric  
Development Plan)**

Dear Dr. Justice,

The sponsor, TAP Pharmaceutical Products Inc. (TAP), submits this amendment to a New Drug Application under the provisions of Section 505(i) of the Federal Food, Drug and Cosmetic Act and 21 CFR § 314.60. The purpose of this amendment is summarized below.

**Chemistry, Manufacturing and Controls**

Enclosed are reports TAP-02-001097-2.0, entitled, "Quality Overall Summary – Drug Product" and TAP-02-000945-2.0, entitled, "Compatibility" that were amended for the following reason:

- To clarify the acceptable total reconstitution time in 0.9% Sodium Chloride is 24 hours. Note that 24-hour stability data was presented in NDA 21-566 and has not changed.

**Labeling**

Since the original labeling for NDA 21-566 for PREVACID® I.V. (lansoprazole) for Injection was submitted on December 20, 2002, the following changes were made to the package insert:

- Moved location of Rx only statement.
- Added the product list number.
- Minor editorial changes.

The following changes were made to both the package insert and the retail carton:

- Decreased the number of vials per carton — to 10.
- Clarified that prior to further dilution, the drug product should only be held in the vial for 1 hour.
- Increased the reconstitution time in the 0.9% Sodium Chloride from 6 } 24 hours.

**Other (Pediatric Development Plan)**

Please find enclosed document TAP-02-001072-2.0 that has been amended to reflect TAP's position on the Pediatric Development Plan.

The enclosed CD-ROM includes documents in .pdf file format as well as the proposed labeling in .doc file format. All electronic files and media (~ 1 MB) provided in this submission have been scanned for computer viruses using McAfee VirusScan version 4.5.0.534 (Network Associates, Inc.).

A complete and accurate copy of this submission has been submitted to Mr. Arlyn H. Baumgarten, District Director of the Chicago Field Office.

Attached is Form FDA 356h to complete this submission. If you have any questions or need additional information please contact me at the number below.

Sincerely,

Nancianne Knipfer, Ph.D.  
Regulatory Product Manager  
847-236-2193  
847-236-2880 (fax)

Attachments

28 Page(s) Withheld

\_\_\_\_\_ § 552(b)(4) Trade Secret / Confidential

\_\_\_\_\_ § 552(b)(5) Deliberative Process

✓ § 552(b)(5) Draft Labeling

DEPARTMENT OF HEALTH AND HUMAN SERVICES PUBLIC HEALTH SERVICE FOOD AND DRUG ADMINISTRATION		<b>REQUEST FOR CONSULTATION</b>		
TO (Division/Office):  <b>Jerry Philips, HFD-400 Parklawn 15B-23</b>		FROM:  Melissa Furness, HFD-180 Parklawn 6B-45		
DATE March 24, 2003	IND NO.	NDA NO. 21-566	TYPE OF DOCUMENT	DATE OF DOCUMENT December 20, 2003
NAME OF DRUG Prevacid IV	PRIORITY CONSIDERATION Standard		CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE August 15, 2003
NAME OF FIRM: Tap Pharmaceutical Products, Inc.				
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 II MEETING <input type="checkbox"/> FINAL PRINTED LABELING <input type="checkbox"/> NEW CORRESPONDENCE <input type="checkbox"/> RESUBMISSION <input type="checkbox"/> LABELING REVISION <input type="checkbox"/> DRUG ADVERTISING <input type="checkbox"/> SAFETY/EFFICACY <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE <input type="checkbox"/> ADVERSE REACTION REPORT <input type="checkbox"/> PAPER NDA <input type="checkbox"/> FORMULATIVE REVIEW <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION <input type="checkbox"/> CONTROL SUPPLEMENT <input type="checkbox"/> OTHER (SPECIFY BELOW): See comments below. <input type="checkbox"/> MEETING PLANNED BY				
<b>COMMENTS/SPECIAL INSTRUCTIONS:</b> This is a type 3 New Drug Application. The PDUFA goal date is 10/23/03. Please note that this application was submitted electronically, consequently, it may be found on the EDR (pathway - N 21566/labeling folder). Please let me know if you require hard copies as well and I can request these from the 'rm. Thanks much! Melissa Furness - x77450.				
SIGNATURE OF REQUESTER		METHOD OF DELIVERY (Check one) <input type="checkbox"/> MAIL <input type="checkbox"/> HAND		
SIGNATURE OF RECEIVER		SIGNATURE OF DELIVERER		

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/s/

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Melissa Furness  
3/24/03 10:20:55 AM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

3-11-03

**NO FILING REVIEW ISSUES IDENTIFIED**

NDA 21-566

TAP Pharmaceutical Products Inc.  
Attention: Nanciane Knipfer, Ph.D.  
Regulatory Product Manager  
675 North Field Drive  
Lake Forest, IL 60045

Dear Dr. Knipfer:

Please refer to your December 20, 2002 new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prevacid I.V. (lansoprazole) Injection 30 mg.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, this application has been filed under section 505(b) of the Act on February 21, 2003 in accordance with 21 CFR 314.101(a).

At this time, we have not identified any potential filing review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review.

If you have any questions, call Melissa Hancock Furness, Regulatory Project Manager, at (301) 827-7450.

Sincerely,

*{See appended electronic signature page}*

Robert L. Justice, M.D., M.S.  
Director  
Division of Gastrointestinal & Coagulation  
Drug Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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/s/

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Robert Justice  
3/11/03 09:40:32 AM

**Division of Gastrointestinal & Coagulation Drug Products**

**ADMINISTRATIVE REVIEW OF NEW DRUG APPLICATION**

**Application Number:** NDA 21-566

**Name of Drug:** Prevacid (lansoprazole) IV

**Sponsor:** Tap Pharmaceuticals

**Date Review Completed:** 02/2003

**Material Reviewed**

**Type of Submission (i.e., paper, electronic, or combination):** electronic

**Submission Date:** 12/20/02

**Receipt Date:** 12/23/02

**Filing Date:** 02/23/03

**User-fee Goal Date(s):** 10/23/03

**Proposed Indication:**

The above listed NDA is proposed for use when patients are unable to take the oral formulations of Prevacid that are currently approved. Prevacid IV for Injection is intended to be an alternative for the short-term treatment (up to 7 days) of all grades of erosive esophagitis.

**Other Background Information:**

TAP has the following oral formulations of Prevacid approved: NDA 20-406 for Prevacid (lansoprazole) Delayed-Release Capsules, NDA 21-281 for Prevacid® (lansoprazole) for Delayed-Release Oral Suspension, and NDA 21-428 for Prevacid® SoluTab (lansoprazole) Delayed-Release Orally Disintegrating Tablet.

**Review**

**PART I: OVERALL FORMATTING<sup>a,d,c</sup>**

[Note: Items 1,2,3,4, & 5 must be submitted in paper.]	Y	N	<b>COMMENTS</b> (If paper: list volume & page numbers) (If electronic: list folder & page numbers)
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1. Cover Letter	x	Cover letter folder
2. Form FDA 356h (original signature)	x	356H folder
a. Establishment information	x	356H folder
b. Reference to DMF(s) & Other Applications	x	356H folder
3. User Fee FDA Form 3397	x	ndatoc.pdf; user fee bookmark and patent info bookmark
4. Patent information & certification		
5. Debarment certification (Note: Must have a definitive statement)	x	ndatoc.pdf/ debarment bookmark
6. Field Copy Certification	x	ndatoc.pdf/ field copy bookmark
7. Financial Disclosure		ndatoc.pdf/ financial disclosure bookmark
8. Comprehensive Index	x	ndatoc.pdf
9. Pagination		N/A due to electronic submission
10. Summary Volume	x	ndatoc.pdf/ summary bookmark
11. Review Volumes	x	
12. Labeling (PI, container, & carton labels)	x	ndatoc.pdf/ labeling bookmark
a. unannotated PI	x	ndatoc.pdf/ labeling bookmark
b. annotated PI	x	ndatoc.pdf/ labeling bookmark
c. immediate container	x	ndatoc.pdf/ labeling bookmark
d. carton	x	ndatoc.pdf/ labeling bookmark
e. patient package insert (PPI)		x N/F
f. foreign labeling (English translation)		x N/F
13. Case Report Tabulations (CRT) (paper or electronic) (by individual patient data listing or demographic)	x	ndatoc.pdf/ crt bookmark
14. Case Report Forms (paper or	x	ndatoc.pdf/ crf bookmark

electronic) (for death & dropouts due to adverse events)			
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Y=Yes (Present), N=No (Absent)

PART II: SUMMARY<sup>b,d,e</sup>

	Y	N	COMMENTS (If paper: list volume & page numbers) (If electronic: list folder & page numbers)
1. Pharmacologic Class, Scientific Rationale, Intended Use, & Potential Clinical Benefits	x		ndatoc.pdf/ summary bookmark
2. Foreign Marketing History		x	N/A
3. Summary of Each Technical Section	x		ndatoc.pdf/ summary bookmark
a. Chemistry, Manufacturing, & Controls (CMC)	x		ndatoc.pdf/ CMC bookmark
b. Nonclinical Pharmacology/Toxicology	x		ndatoc.pdf/ pharmtox bookmark
c. Human Pharmacokinetic & Bioavailability	x		ndatoc.pdf/ hpbio bookmark
d. Microbiology		x	N/A
e. Clinical Data & Results of Statistical Analysis	x		ndatoc.pdf/ clinstat bookmark
4. Discussion of Benefit/Risk Relationship & Proposed Postmarketing Studies	x		ndatoc.pdf/ summary bookmark
5. Summary of Safety	x		ndatoc.pdf/ summary bookmark
6. Summary of Efficacy	x		ndatoc.pdf/ summary bookmark

Y=Yes (Present), N=No (Absent)

PART III: CLINICAL/STATISTICAL SECTIONS<sup>c,d,e</sup>

	Y	N	COMMENTS (If paper: list volume & page numbers) (If electronic: list folder & page numbers)

1. List of Investigators	x		ndatoc.pdf/ clinstat bookmark
2. Controlled Clinical Studies			
a. Table of all studies	x		clinstat folder/ clintoc.pdf
b. Synopsis, protocol, related publications, list of investigators, & integrated clinical & statistical report for each study (including completed, ongoing, & incomplete studies)		x	N/F
c. Optional overall summary & evaluation of data from controlled clinical studies		x	N/F
3. Integrated Summary of Efficacy (ISE)	x		clinstat folder/ ise folder
4. Integrated Summary of Safety (ISS)	x		clinstat folder/ iss folder
5. Drug Abuse & Overdosage Information	x		Integrated in ISS
6. Integrated Summary of Benefits & Risks of the Drug	x		Summary folder; Overall Clinical Summary folder
7. Gender/Race/Age Safety & Efficacy Analysis of Studies		x	N/F

Y=Yes (Present), N=No (Absent)

PART IV: MISCELLANEOUS<sup>d,e</sup>

	Y	N	COMMENTS (list volume & page numbers) (If electronic: list folder & page numbers)
1. Written Documentation Regarding Drug Use in the Pediatric Population		x	N/F

2. Review Aids (Note: In electronic submission, can only request aids if increase functionality. In paper submission, verify that aids contain the exact information duplicated on paper. Otherwise, the aids are considered electronic submissions.)			See a-e  Electronic-submission, therefore, none requested
a. Proposed unannotated labeling in MS WORD	x		Label folder/ proposed.doc
b. Stability data in SAS data set format (only if paper submission)		x	N/A
c. Efficacy data in SAS data set format (only if paper submission)		x	N/A
d. Biopharmacological information & study summaries in MS WORD (only if paper submission)		x	N/A (electronic)
e. Animal tumorigenicity study data in SAS data set format (only if paper submission)		x	N/A
3. Exclusivity Statement (optional)		x	N/F

Y=Yes (Present), N=No (Absent)

<sup>a</sup>•GUIDELINE ON FORMATTING, ASSEMBLING, AND SUBMITTING NEW DRUG AND ANTIBIOTIC APPLICATIONS••(FEBRUARY 1987).

<sup>b</sup>•GUIDELINE FOR THE FORMAT AND CONTENT OF THE SUMMARY FOR NEW DRUG AND ANTIBIOTIC APPLICATIONS••(FEBRUARY 1987).

<sup>c</sup>•GUIDELINE FOR THE FORMAT AND CONTENT OF THE CLINICAL AND STATISTICAL SECTIONS OF NEW DRUG APPLICATIONS••(JULY 1988).

<sup>d</sup>“GUIDANCE FOR INDUSTRY: PROVIDING REGULATORY SUBMISSIONS IN ELECTRONIC FORMAT-GENERAL CONSIDERATIONS” (JANUARY 1999).

<sup>e</sup>“GUIDANCE FOR INDUSTRY: PROVIDING REGULATORY SUBMISSIONS IN ELECTRONIC FORMAT-NDAS” (JANUARY 1999).

Melissa Hancock Furness  
Regulatory Project Manager  
02/2003

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/s/

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Melissa Furness  
10/16/03 11:37:47 AM  
CSO

**REQUEST FOR CONSULTATION**

TO (Division/Office):  <b>Peter Cooney, Ph.D., HFD-805</b> <b>Parklawn Building, 18B-08</b>	FROM:  Melissa Hancock Furness, B.S., HFD-180 Parklawn Building 6B-45
--	--

DATE January 22, 2003	IND NO.	NDA NO. 21-566	TYPE OF DOCUMENT	DATE OF DOCUMENT December 23, 2002
NAME OF DRUG Prevacid IV		PRIORITY CONSIDERATION Standard	CLASSIFICATION OF DRUG	DESIRED COMPLETION DATE September 2003

NAME OF FIRM: Tap Pharmaceutical Products, Inc.

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 II MEETING | <input type="checkbox"/> FINAL PRINTED LABELING        |
| <input type="checkbox"/> NEW CORRESPONDENCE            | <input type="checkbox"/> RESUBMISSION            | <input type="checkbox"/> LABELING REVISION             |
| <input type="checkbox"/> DRUG ADVERTISING              | <input type="checkbox"/> SAFETY/EFFICACY         | <input type="checkbox"/> ORIGINAL NEW CORRESPONDENCE   |
| <input type="checkbox"/> ADVERSE REACTION REPORT       | <input type="checkbox"/> PAPER NDA               | <input type="checkbox"/> FORMULATIVE REVIEW            |
| <input type="checkbox"/> MANUFACTURING CHANGE/ADDITION | <input type="checkbox"/> CONTROL SUPPLEMENT      | <input type="checkbox"/> OTHER (SPECIFY BELOW):        |
| <input type="checkbox"/> MEETING PLANNED BY            |  | <input type="checkbox"/> See comments below            |

**COMMENTS/SPECIAL INSTRUCTIONS:** This is a new NDA for Prevacid IV. The Microbiology volumes are being delivered to you from the document room. Please let me know the name of the Microbiology reviewer assigned to this NDA so that I can include them in all future meetings.

SIGNATURE OF REQUESTER: Melissa Hancock Furness	METHOD OF DELIVERY (Check one) <input type="checkbox"/> MAIL <input type="checkbox"/> HAND
SIGNATURE OF RECEIVER	SIGNATURE OF DELIVERER

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/s/

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Melissa Furness

1/22/03 10:40:29 AM



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-566

1-22-03

TAP Pharmaceutical Products Inc.  
Attention: Nanciane Knipfer, Ph.D.  
Regulatory Product Manager  
675 North Field Drive  
Lake Forest, IL 60045

Dear Dr. Knipfer:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Prevacid I.V. (lansoprazole) Injection 30 mg

Review Priority Classification: Standard (S)

Date of Application: December 20, 2002

Date of Receipt: December 23, 2002

Our Reference Number: NDA 21-566

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on February 21, 2003 in accordance with 21 CFR 314.101(a). If the application is filed, the user fee goal date will be October 23, 2003.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application. Address all communications concerning this NDA as follows:

U.S. Postal/Courier/Overnight Mail:  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Gastrointestinal and Coagulation Drug Products, HFD-180  
Attention: Division Document Room 8B-45  
5600 Fishers Lane  
Rockville, Maryland 20857

NDA 21-566

Page 2

If you have any questions, call me at (301) 827-7450.

Sincerely,

*{See appended electronic signature page}*

Melissa Hancock Furness  
Consumer Safety Officer  
Division of Gastrointestinal and  
Coagulation Drug Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

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/s/

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Melissa Furness  
1/22/03 10:52:45 AM

**New Drug Application  
Electronic Media for Archive**

December 20, 2002

Robert Justice, M.D.  
Director  
Division of Gastrointestinal and Coagulation Drug Products, HFD-180  
Document Control Room 6B-45  
Center for Drug Evaluation and Research  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

**NDA 21-566**

**PREVACID® I.V. (lansoprazole) for Injection, 30 mg**

Dear Dr. Justice,

The sponsor, TAP Pharmaceutical Products Inc. (TAP), submits this New Drug Application (NDA) in accordance with section 505(b)(1) of the Federal Food, Drug and Cosmetic Act and Title 21 CFR § 314.50, to NDA 21-566 for PREVACID® I.V. (lansoprazole) for Injection, 30 mg. PREVACID® I.V. (lansoprazole) for Injection has the same active pharmaceutical ingredient as NDA 20-406, NDA 21-281 and NDA 21-428 for PREVACID® (lansoprazole) Delayed-Release Capsules, PREVACID® (lansoprazole) For Delayed-Release Oral Suspension and PREVACID® SoluTab™ (lansoprazole) Delayed-Release Orally Disintegrating Tablets, respectively.

The proposed labeling for this NDA is supported by the pharmacokinetic, pharmacodynamic and safety results of two pivotal (M01-308 and M01-307) and two supportive (M95-306 and M96-486) domestic clinical trials. Proposed study designs for the pivotal studies were agreed upon by the Agency on June 13, 2001. Additional safety data is provided from 27 foreign clinical studies.

The proposed indication is:

When patients are unable to take the oral formulations, PREVACID® I.V. for Injection is indicated as an alternative for the short-term treatment (up to 7 days) of all grades of erosive esophagitis.

PREVACID® I.V. (lansoprazole) for Injection, 30 mg will be supplied in cartons of — glass vials. An expiration date of 36 months is proposed.

NDA 21-566  
PREVACID® I.V. (lansoprazole) for Injection  
December 20, 2002  
Page 2 of 2

This NDA consists of 46 paper volumes and 2 CD-ROMs containing pdf files and a copy of the proposed labeling in Microsoft Word. All electronic files and media provided in this submission have been scanned for computer viruses using McAfee VirusScan version 4.5.1 Service Pack 1 (Network Associates, Inc.).

A complete and accurate copy of Items 1.0 - 4.0 of this NDA has been submitted to Mr. Arlyn H. Baumgarten, District Director of the Chicago Field Office.

Attached is Form FDA 356h to complete this submission. If you have any questions or need additional information please contact me at the number below.

Sincerely,

Nancianne Knipfer, Ph.D.  
Regulatory Product Manager  
847-236-2193  
847-236-2880 (fax)

Attachments

27 Page(s) Withheld

\_\_\_\_\_ § 552(b)(4) Trade Secret / Confidential

\_\_\_\_\_ § 552(b)(5) Deliberative Process

\_\_\_\_\_ § 552(b)(5) Draft Labeling