

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-281

CORRESPONDENCE



TAP HOLDINGS INC.
parent of TAP Pharmaceuticals Inc.

Hannockburn Lake Office Plaza
2355 Waukegan Rd.
Deerfield, IL 60015

June 30, 2000

Division of Gastrointestinal and Coagulation Drug Product, HFD-180
Document Control Room 6B-24
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Attention: Lilia Talarico, M.D.
Director

Re: PREVACID® (lansoprazole) Sachet for Suspension
NDA 21-281
User Fee ID# 3963

Dear Dr. Talarico:

Pursuant to Section 505(b) of the Federal Food, Drug and Cosmetic Act and 21 CFR Part 314.50, the Sponsor, TAP Pharmaceutical Products Inc., is submitting a New Drug Application (NDA #21-281) for PREVACID® Sachet for Suspension (lansoprazole).

PREVACID Sachet for Suspension, which was developed for patients who have difficulty swallowing capsules, is a lansoprazole new dosage form and will have the same indications as PREVACID (lansoprazole) Delayed-Release Capsules (NDA# 20-406). This new dosage form of PREVACID will be supplied as 15 mg and 30 mg unit dose sachets.

Each PREVACID sachet unit dose is comprised of enteric-coated lansoprazole granules, identical to those in the currently marketed PREVACID (lansoprazole) Delayed-Release capsules, along with inactive granules. The lansoprazole granules are manufactured at _____ and the inactive granules which are comprised of thickening, sweetening, coloring and flavoring agents are manufactured at _____. The sachet finished drug product is also manufactured at _____. Each unit dose sachet is reconstituted into a suspension with approximately 30 ml of water and is administered orally.

This NDA is supported by two studies M98-944 and M98-945 to demonstrate bioequivalence between the PREVACID Sachet for Suspension and PREVACID (lansoprazole) Delayed-Release Capsules. The submission also contains four review copies of the Chemistry Manufacturing Controls (CMC) data and a CD Rom containing data listings, SAS data sets and labeling information for the product.

7/7/00 Comment put in DSS

60 days = 9/1/00 Fri

10 mo = 5/3/01 Th

12 mo = 7/3/01 Tu





June 30, 2000
Page 2 of 2

TAP Pharmaceutical Products Inc. certifies that to the best of our knowledge, we did not and will not use in any capacity the services of any person debarred under Section 306(a) or (b) of the Federal Food, Drug and Cosmetic Act in connection with this New Drug Application.

In accordance with the Prescription Drug User Fee Act, a check for the applicable user fee for this application _____ was remitted on June 16, 2000.

Product samples of PREVCID® Sachet for Suspension will be supplied to the Agency when requested.

We look forward to working with the Division on this NDA. Please direct any questions on this application to the undersigned.

Sincerely,

A handwritten signature in cursive script that reads 'Betsy A. Brown'.

Betsy A. Brown
Assistant Director, Regulatory Affairs
Telephone: (847-317-5781)
Fax: (847) 317-5795



DEPARTMENT OF HEALTH & HUMAN SERVICES

Derry

NDA 21-281

Food and Drug Administration
Rockville MD 20857

TAP Pharmaceutical Products Inc.
Attention: Ms. Betsy Brown
Assitant Director, Regulatory Affairs
675 North Field Drive
Lake Forest, IL 60045

AUG - 1 2000

Dear Ms. Brown:

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® (lansoprazole) Sachet for Suspension
Therapeutic Classification: Standard (S)
Date of Application: June 30, 2000
Date of Receipt: July 3, 2000
Our Reference Number: NDA 21-281

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on September 1, 2000 in accordance with 21 CFR 314.101(a). If the application is filed, the primary user fee goal date will be May 3, 2001 and the secondary user fee goal date will be July 3, 2001.

Be advised that, as of April 1, 1999, 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 (63 FR 66632). If you have not already fulfilled the requirements of 21 CFR 314.55 (or 601.27), please submit your plans for pediatric drug development within 120 days from the date of this letter unless you believe a waiver is appropriate. Within approximately 120 days of receipt of your pediatric drug development plan, we will review your plan and notify you of its adequacy.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will make a determination whether to grant or deny a request for a waiver of pediatric studies during the review of the application. In no case, however, will the determination be made later than the date action is taken on the application. If

a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov/cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" (PPSR) in addition to your plans for pediatric drug development described above. We recommend that you submit a Proposed Pediatric Study Request within 120 days from the date of this letter. If you are unable to meet this time frame but are interested in pediatric exclusivity, please notify the division in writing. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. If you do not submit a PPSR or indicate that you are interested in pediatric exclusivity, we will review your pediatric drug development plan and notify you of its adequacy. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

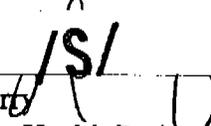
Please cite the NDA number listed above at the top of the first page of any communications concerning this application. All communications concerning this NDA should be addressed as follows:

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, 6B-45
5600 Fishers Lane
Rockville, Maryland 20857

If you have any questions, call me at (301) 827-7475.

Sincerely,


Cheryl Perry
Regulatory Health Project Manager
Division of Gastrointestinal and Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research



NDA 21-281

DISCIPLINE REVIEW LETTER

TAP Pharmaceutical Products, Inc.
Attention: Betsy A. Brown
Assistant Director, Regulatory Affairs
675 North Field Drive
Lake Forest, IL 60045

NOV 16 2000

Dear Ms. Brown:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prevacid[®] Sachet for Suspension (lansoprazole) 15 mg and 30 mg.

Our review of the Clinical Pharmacology and Biopharmaceutics section of your submission is complete, and we have identified the following deficiencies:

1. Please provide complete tabulated acid resistance data, tabulated and graphical drug release profile for each dose unit of the Prevacid[®] sachet tested for acid resistance and for drug release (NDA Volume 1.11 [pages 044-045]).
2. Please justify the use of _____ for drug release testing of the Prevacid[®] sachet formulations versus _____ for the Prevacid[®] capsule formulation.

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 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 Cheryl Perry, Regulatory Health Project Manager, at (301) 827-7475.

Sincerely,

Kati Johnson
Supervisory Consumer Safety Officer
Division of Gastrointestinal and Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

/s/

Kati Johnson

(11/16/00 11:27:42 AM



NDA 21-281

DISCIPLINE REVIEW LETTER

TAP Pharmaceutical Products, Inc.
Attention: Betsy A. Brown
675 North Field Drive
Lake Forest, IL 60045

MAR -5 2001

Dear Ms. Brown:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prevacid® (lansoprazole) Sachet for Suspension, 15 mg and 30 mg.

We also refer to your submission dated November 30, 2000, in response to our Discipline Review letter dated November 16, 2001, requesting information regarding acid resistance data, drug release profile, and the use of 0.1 M borate buffer for drug release testing.

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

[Redacted content]

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 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 Cheryl Perry, Regulatory Health Project Manager, at (301) 827-7475.

Sincerely,

Juliann DuBeau, RN, MSN
Chief, Project Management Staff
Division of Gastrointestinal and Coagulation Drug Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

/s/

Julie DuBeau

(3/5/01 04:39:10 PM



FAX

United States Food and Drug Administration
 Division of Gastrointestinal and Coagulation Drug Products
 Parklawn, Room 6B-45, HFD-180
 5600 Fishers Lane
 Rockville, MD 20857

MAR 14 2001

Date: March 14, 2001

/S/

To: Ms. Betsy Brown Associate Director, Regulatory Affairs TAP Pharmaceutical Products, Inc.	From: Ms. Cheryl Perry Regulatory Health Project Manager Div. of Gastrointestinal & Coagulation Drugs, HFD-180
Tel: (847) 317-5781	Tel: 301-827-7475
Fax: (847) 236-2892 847-236-2880	Fax: 301-443-9285

Total No. Of Pages: 4 Including Cover

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Re: NDA 21-281 CMC Information Request Letter

Hello Betsy,

As per my voicemail today, please submit to NDA 21-281, your proposed color mock-up labels for the sachet packet (immediate container), and the unit-dose carton for the 15-mg and 30-mg drug products as soon as possible.

Thank you,

/S/



MAR 14 2001

NDA 21-281

INFORMATION REQUEST LETTER

TAP Pharmaceutical Products, Inc.
Attention: Ms. Betsy A. Brown
675 North Field Drive
Lake Forest, IL 60045

Dear Ms. Brown:

Please refer to your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Prevacid® (lansoprazole) Sachet for Suspension, 15 mg and 30 mg.

We are reviewing the Chemistry, Manufacturing and Controls (CMC) section of your submission and have the following comments and information requests. We need your prompt written response to continue our evaluation of your NDA.

1. With respect to Prevacid Sachet's "Regulatory Specifications and Test Methods":
 - a. Provide an infrared (IR) identity test under the "Identification" heading, in addition to your proposed retention time test.
 - b. Provide the identity of lansoprazole degradants contributing to the in the "Acid resistance" test and appropriately adjust the lansoprazole results for the absorbance contribution of the lansoprazole degradants.
2. Provide a specification for specified and total degradants for Prevacid Sachet (15 and 30 mg). Further, the terms "Sum of Other Related Substances" and "Related Substances" in the stability protocols should accurately reflect the fact that they are in reference to degradants.
3. Provide updated stability data to support the proposed two-year expiry dating period.
4. Designate the potency for the first three production batches, i.e., three production batches of 15 mg sachets and three production batches of 30 mg sachets, in the "Post Approval Stability Commitment".
5. Provide accelerated conditions in the "Post Approval Stability Protocol".
6. Submit a Methods Validation Package after completion of the changes to the chemistry, manufacturing and controls for Prevacid Sachet.

NDA 21-281
Information Request

If you have any questions, call Cheryl Perry, Regulatory Health Project Manager, at (301) 827-7475.

Sincerely,

{See appended electronic signature page}

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



TAP PHARMACEUTICAL PRODUCTS INC.

675 North First Drive
Lake Forest, IL 60045

April 25, 2001

Lilia Talarico, M.D.
Director
Division of Gastrointestinal and Coagulation Drug Products, HFD-180
Document Control Room 6B-24
Center for Drug Evaluation and Research
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

**Re: PREVACID® (lansoprazole delayed-release granules for oral suspension)
NDA 21-281**

Dear Dr. Talarico:

Please reference NDA 21-281 PREVACID (lansoprazole delayed-release granules for oral suspension) and the April 25, 2001 telephone discussion between Cheryl Perry, FDA Project Manager, and Betsy Brown of TAP Pharmaceutical Products Inc. concerning the proposed Established Name for the aforementioned product.

TAP Pharmaceutical Products Inc. authorizes the Agency to contact the United States Pharmacopoeia to discuss the finalization of the proposed Established Name for NDA 21-281 PREVACID (lansoprazole delayed-release granules for oral suspension).

If you have any questions concerning this matter, please do not hesitate to contact me.

As always, we thank the Agency for their much valued time and support.

Sincerely,

A handwritten signature in cursive script that reads "Betsy A. Brown".

Betsy A. Brown
Associate Director, Regulatory Affairs
847-317-5781

cc: Dr. Liang Zhou