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APPLICATION NUMBER: 050757/S02

MEDICAL REVIEW(S)

JAN 2 2 1999

NDA 50-757 002

Medical Officer Review of Efficacy Supplement

Submission Date:	October 5, 1998
Review complete:	December 7, 1998
Applicant:	TAP Holdings Inc 2355 Waukengan Road Deerfield, IL 60015
Drug:	Trade: PREVPAC Generic: Lansoprazole
Dosage form:	tablet
Route of administration:	oral
Contents of submission:	One volume

Purpose of submission:

- To update the lansoprazole label and incorporate minor changes to the BIAXIN information contained in the PREVPAC package insert due to a recent revision to the BIAXIN package insert.
- To add a NDC code for the daily administration card for PREVPAC, NDC 0300-3701-11, under the **HOW SUPPLIED** section
- To change the **HOW SUPPLIED** section of the label which reads "Caution: Federal (USA) law prohibits dispensing without a prescription" to "RX only" as per 1998 Modernization Act.

Proposed labeling:

A number of changes have been made which incorporates recent changes to the BIAXIN label:

- Under the drug interaction section of the label that describes clarithromycin drug-drug interactions, the words "potentially fatal" are inserted to describe arrhythmias which can occur when clarithromycin is given concurrently with digoxin. The change was made to be consistent with the current BIAXIN package insert.
- Under the same section, the following statement was added to describe clarithromycin interactions with HMG-CoA reductase inhibitors. The following statement has been included: "As with other macrolides, clarithromycin has been reported to increase concentrations of HMG-CoA reductase inhibitors (e.g., lovastatin and simvastatin), through inhibition of cytochrome P450 metabolism of these drugs. Rare reports of rhabdomyolysis have been reported in patients taking these drugs concomitantly." In addition, rifabutin was added to the list of drugs that have associated elevations in serum levels when given concurrently with erythromycin and clarithromycin.
- Under the post marketing section of the label, the words "thrombocytopenia", "leukopenia", "neutropenia", "taste loss", "manic behavior" and "tremor" were added to the list to be consistent with the BIAXIN package insert. The following statement was also added: "There have been rare reports of hypoglycemia, some of which have occurred in patients taking oral hypoglycemic agents or insulin." Again, this statement was incorporated to be consistent with the BIAXIN package insert.
- Under the HOW SUPPLIED section, a NDC code for daily administration card was added and the phrase "Caution: Federal (USA) law prohibits dispensing without a prescription" was changed to "RX only" as per the 1998 Modernization Act.

Medical Officer's Comment: These changes are considered acceptable.

The MICROBIOLOGY section, CLINICAL STUDIES section, ADVERSE REACTIONS section, and DOSAGE AND ADMINISTRATION section have been previously reviewed and approved (See FDA approval letter for NDA 20-406/S-021 dated July 20, 1995 by Dr. Lilia Talarico (Div of

Gastrointestinal and Coagulation Drug Products). Please also see Medical/Statistical Review (dated Dec 12, 1997) for NDA 20-406/s-021 reviewed one clinical study evaluating 14-day triple therapy versus 10-day triple therapy. These labeling changes include the following:

- A more detailed analysis of the susceptibility results for all studies using lansoprazole in combination for *H. pylori* has been incorporated into the **MICROBIOLOGY** section.
- Eradication rates for the 10-day triple therapy lansoprazole regimen is incorporated into the CLINICAL STUDIES section.
- A statement that there were no statistically significant difference in the frequency of reported adverse events between the 10- and 14-day triple therapy regimens has been incorporated into the **ADVERSE REACTIONS** section
- The addition of 10-days to the triple therapy **DOSE AND ADMINISTRATIONS** section for H. pylori eradication

Medical Officer's Comment: These labeling changes are acceptable.

Additional changes have been made to the Prevecid label since approval of the original Prevecid package (NDA-20-406):

- The ADVERSE REACTION section now states that anaphylactoid-like reactions can occur.
- The ADVERSE REACTION section has changes the word "amblyopia" to "blurred vision".

Medical Officer's Comment: These changes are acceptable

A NDC code for the daily administration card for PREVPAC, NDC 0300-3701-11, under the **HOW SUPPLIED** section has also been included. The **HOW SUPPLIED** section of the label which reads "Caution: Federal (USA) law prohibits dispensing without a prescription" has also been changed to read "RX only" as per 1998 Modernization Act.

Medical Officer's Comment: These changes are acceptable

Medical Officer's Recommendations
The sponsor should be notified that the proposed changes to the label are acceptable.

/S/

Robert Hopkins M.D., M.P.H. & T.M.
Medical Team Leader, DSPIDP

Concurrence:
HFD-590/DivDir/GoldbergerM /S/ 'h/m

APPEARS THIS WAY
ON ORIGINAL

CC
NDA 50-757
HFD-590/PM/AndersonR
HFD-590/MTL/Hopkins