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PREVACID®

(lansoprazole)
Delayed-Release Capsules

PREVACID®

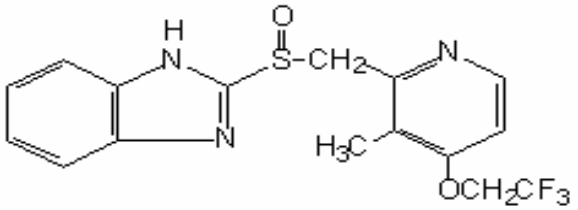
(lansoprazole)
For Delayed-Release Oral Suspension

PREVACID® SoluTab™

(lansoprazole)
Delayed-Release Orally Disintegrating Tablets

DESCRIPTION

The active ingredient in PREVACID Delayed-Release Capsules, PREVACID for Delayed-Release Oral Suspension and PREVACID SoluTab Delayed-Release Orally Disintegrating Tablets is lansoprazole, a substituted benzimidazole, 2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridyl] methyl] sulfinyl] benzimidazole, a compound that inhibits gastric acid secretion. Its empirical formula is $C_{16}H_{14}F_3N_3O_2S$ with a molecular weight of 369.37. PREVACID has the following structure:



Lansoprazole is a white to brownish-white odorless crystalline powder which melts with decomposition at approximately 166°C. Lansoprazole is freely soluble in dimethylformamide; soluble in methanol; sparingly soluble in ethanol; slightly soluble in ethyl acetate, dichloromethane and acetonitrile; very slightly soluble in ether; and practically insoluble in hexane and water.

Lansoprazole is stable when exposed to light for up to two months. The rate of degradation of the compound in aqueous solution increases with decreasing pH. The degradation half-life of the drug substance in aqueous solution at 25°C is approximately 0.5 hour at pH 5.0 and approximately 18 hours at pH 7.0.

PREVACID is supplied in delayed-release capsules, in delayed-release orally disintegrating tablets for oral administration and in a packet for delayed-release oral suspension.

The delayed-release capsules are available in two dosage strengths: 15 mg and 30 mg of lansoprazole per capsule. Each delayed-release capsule contains enteric-coated granules consisting of 15 mg or 30 mg of lansoprazole (active ingredient) and the following inactive ingredients: hydroxypropyl cellulose, low substituted hydroxypropyl cellulose, colloidal silicon dioxide, magnesium carbonate, methacrylic acid copolymer, starch, talc, sugar sphere, sucrose, polyethylene glycol, polysorbate 80, and titanium dioxide. Components of the gelatin capsule include gelatin, titanium dioxide, D&C Red No. 28, FD&C Blue No. 1, FD&C Green No. 3*, and FD&C Red No. 40 (inactive ingredients).

PREVACID SoluTab Delayed-Release Orally Disintegrating Tablets are available in two dosage strengths: 15 mg and 30 mg of lansoprazole per tablet. Each delayed-release orally disintegrating tablet contains enteric-coated microgranules consisting of 15 mg or 30 mg of lansoprazole (active ingredient) and the following inactive ingredients: lactose monohydrate, microcrystalline cellulose, magnesium carbonate, hydroxypropyl cellulose, hypromellose, titanium dioxide, talc, mannitol, methacrylic acid, polyacrylate, polyethylene glycol, glyceryl monostearate, polysorbate 80, triethyl citrate, ferric oxide, citric acid, crospovidone, aspartame **, artificial strawberry flavor and magnesium stearate.

PREVACID for Delayed-Release Oral Suspension are available in two dosage strengths: 15 mg and 30 mg of lansoprazole per packet. Each packet of delayed-release oral suspension contains enteric-coated granules consisting of 15 or 30 mg of lansoprazole (active ingredient) and the following inactive ingredients (inactive granules): confectioner's sugar, mannitol, docusate sodium, ferric oxide, colloidal silicon dioxide, xanthan gum, crospovidone, citric acid, sodium citrate, magnesium stearate, and artificial strawberry flavor. The lansoprazole granules and inactive granules, present in unit dose packets, are constituted with water to form a suspension and consumed orally.

* PREVACID 15-mg capsules only.
** **Phenylketonurics: Contains Phenylalanine 2.5 mg per 15 mg Tablet and 5.1 mg per 30 mg Tablet.**

CLINICAL PHARMACOLOGY

Pharmacokinetics and Metabolism

PREVACID Delayed-Release Capsules, PREVACID SoluTab Delayed-Release Orally Disintegrating Tablets and PREVACID for Delayed-Release Oral Suspension contain an enteric-coated granule formulation of lansoprazole. Absorption of lansoprazole begins only after the granules leave the stomach. Absorption is rapid, with mean peak plasma levels of lansoprazole occurring after approximately 1.7 hours. After a single-dose administration of 15 mg to 60 mg of oral lansoprazole, the peak plasma concentrations (C_{max}) of lansoprazole and the area under the plasma concentration curves (AUCs) of lansoprazole were approximately proportional to the administered dose. Lansoprazole does not accumulate and its pharmacokinetics are unaltered by multiple dosing.

Absorption

The absorption of lansoprazole is rapid, with the mean C_{max} occurring approximately 1.7 hours after oral dosing, and the absolute bioavailability is over 80%. In healthy subjects, the mean (±SD) plasma half-life was 1.5 (±1.0) hours. Both the C_{max} and AUC are diminished by about 50% to 70% if lansoprazole is given 30 minutes after food, compared to the fasting condition. There is no significant food effect if lansoprazole is given before meals.

Distribution
Lansoprazole is 97% bound to plasma proteins. Plasma protein binding is constant over the concentration range of 0.05 to 5.0 µg/mL.

Metabolism
Lansoprazole is extensively metabolized in the liver. Two metabolites have been identified in measurable quantities in plasma (the hydroxylated sulfinyl and sulfone derivatives of lansoprazole). These metabolites have very little or no antisecretory activity. Lansoprazole is thought to be transformed into two active species which inhibit acid secretion by blocking the proton pump [(H^+,K^+)-ATPase enzyme system] at the secretory surface of the gastric parietal cell. The two active species are not present in the systemic circulation. The plasma elimination half-life of lansoprazole is less than 2 hours while the acid inhibitory effect lasts more than 24 hours. Therefore, the plasma elimination half-life of lansoprazole does not reflect its duration of suppression of gastric acid secretion.

Elimination
Following single-dose oral administration of PREVACID, virtually no unchanged lansoprazole was excreted in the urine. In one study, after a single oral dose of ^{14}C-lansoprazole, approximately one-third of the administered radiation was excreted in the urine and two-thirds was recovered in the feces. This implies a significant biliary excretion of the lansoprazole metabolites.

Special Populations

Geriatric
The clearance of lansoprazole is decreased in the elderly, with elimination half-life increased approximately 50% to 100%. Because the mean half-life in the elderly remains between 1.9 to 2.9 hours, repeated once daily dosing does not result in accumulation of lansoprazole. Peak plasma levels were not increased in the elderly. No dosage adjustment is necessary in the elderly.

Pediatric
The pharmacokinetics of lansoprazole were studied in pediatric patients with GERD aged 1 to 11 years and 12 to 17 years in two separate clinical studies. In children aged 1 to 11 years, lansoprazole was dosed 15 mg daily for subjects weighing ≤ 30 kg and 30 mg daily for subjects weighing greater than 30 kg. Mean C_{max} and AUC values observed on Day 5 of dosing were similar between the two dose groups and were not affected by weight or age within each weight-adjusted dose group used in the study. In adolescent subjects aged 12 to 17 years, subjects were randomized to receive lansoprazole at 15 mg or 30 mg daily. Mean C_{max} and AUC values of lansoprazole were not affected by body weight or age; and nearly dose-proportional increases in mean C_{max} and AUC values were observed between the two dose groups in the study. Overall, lansoprazole pharmacokinetics in pediatric patients aged 1 to 17 years were similar to those observed in healthy adult subjects.

Gender

In a study comparing 12 male and 6 female human subjects who received lansoprazole, no gender differences were found in pharmacokinetics and intragastric pH results. (Also see **Use in Women**).

Renal Insufficiency

In patients with severe renal insufficiency, plasma protein binding decreased by 1.0%-1.5% after administration of 60 mg of lansoprazole. Patients with renal insufficiency had a shortened elimination half-life and decreased total AUC (free and bound). The AUC for free lansoprazole in plasma, however, was not related to the degree of renal impairment; and the C_{max} and T_{max} (time to reach the maximum concentration) were not different than the C_{max} and T_{max} from subjects with normal renal function. No dosage adjustment is necessary in patients with renal insufficiency.

Hepatic Insufficiency

In patients with various degrees of chronic hepatic disease, the mean plasma half-life of lansoprazole was prolonged from 1.5 hours to 3.2-7.2 hours. An increase in the mean AUC of up to 500% was observed at steady state in hepatically-impaired patients compared to healthy subjects. Dose reduction in patients with severe hepatic disease should be considered.

Race

The pooled mean pharmacokinetic parameters of PREVACID from twelve U.S. Phase 1 studies (N=513) were compared to the mean pharmacokinetic parameters from two Asian studies (N=20). The mean AUCs of PREVACID in Asian subjects were approximately twice those seen in pooled U.S. data; however, the inter-individual variability was high. The C_{max} values were comparable.

Pharmacodynamics

Mechanism of Action

PREVACID (lansoprazole) belongs to a class of antisecretory compounds, the substituted benzimidazoles, that suppress gastric acid secretion by specific inhibition of the (H^+,K^+)-ATPase enzyme system at the secretory surface of the gastric parietal cell. Because this enzyme system is regarded as the acid (proton) pump within the parietal cell, lansoprazole has been characterized as a gastric acid-pump inhibitor, in that it blocks the final step of acid production. This effect is dose-related and leads to inhibition of both basal and stimulated gastric acid secretion irrespective of the stimulus. Lansoprazole does not exhibit anticholinergic or histamine type-2 antagonist activity.

Antisecretory Activity

After oral administration, lansoprazole was shown to significantly decrease the basal acid output and significantly increase the mean gastric pH and percent of time the gastric pH was greater than 3 and greater than 4. Lansoprazole also significantly reduced meal-stimulated gastric acid output and secretion volume, as well as pentagastrin-stimulated acid output. In patients with hypersecretion of acid, lansoprazole significantly reduced basal and pentagastrin-stimulated gastric acid secretion. Lansoprazole inhibited the normal increases in secretion volume, acidity and acid output induced by insulin.

The intragastric pH results of a five-day, pharmacodynamic, crossover study of 15 mg and 30 mg of once daily lansoprazole are presented in Table 1:

Table 1: Mean Antisecretory Effects After Single and Multiple Daily PREVACID Dosing

		PREVACID			
	Baseline	15 mg		30 mg	
Parameter	Value	Day 1	Day 5	Day 1	Day 5
Mean 24-Hour pH	2.1	2.7[+]	4.0[+]	3.6[*]	4.9[*]
Mean Nighttime pH	1.9	2.4	3.0[+]	2.6	3.8[*]
% Time Gastric pH>3	18	33[+]	59[+]	51[*]	72[*]
% Time Gastric pH>4	12	22[+]	49[+]	41[*]	66[*]

NOTE: An intragastric pH of greater than 4 reflects a reduction in gastric acid by 99%.
[*]($p<0.05$) versus baseline and lansoprazole 15 mg.
[+]($p<0.05$) versus baseline only.

After the initial dose in this study, increased gastric pH was seen within 1-2 hours with 30 mg of lansoprazole and 2-3 hours with 15 mg of lansoprazole. After multiple daily dosing, increased gastric pH was seen within the first hour post-dosing with 30 mg of lansoprazole and within 1-2 hours post-dosing with 15 mg of lansoprazole.

Acid suppression may enhance the effect of antimicrobials in eradicating *Helicobacter pylori (H. pylori).* The percentage of time gastric pH was elevated above 5 and 6 was evaluated in a crossover study of PREVACID given daily, b.i.d. and t.i.d (Table 2).

Table 2: Mean Antisecretory Effects After 5 Days of b.i.d. and t.i.d. Dosing

	PREVACID			
Parameter	30 mg daily	15 mg b.i.d.	30 mg b.i.d.	30 mg t.i.d.
% Time Gastric pH>5	43	47	59[+]	77[*]
% Time Gastric pH>6	20	23	28	45[*]

[+]($p<0.05$) versus PREVACID 30 mg daily
[*]($p<0.05$) versus PREVACID 30 mg daily, 15 mg b.i.d. and 30 mg b.i.d.

The inhibition of gastric acid secretion as measured by intragastric pH gradually returned to normal over two to four days after multiple doses. There was no indication of rebound gastric acidity.

Enterochromaffin-like (ECL) Cell Effects

During lifetime exposure of rats with up to 150 mg/kg/day of lansoprazole dosed seven days per week, marked hypergastrinemia was observed followed by ECL cell proliferation and formation of carcinoid tumors, especially in female rats (see **PRECAUTIONS, Carcinogenesis, Mutagenesis, Impairment of Fertility**).

Gastric biopsy specimens from the body of the stomach from approximately 150 patients treated continuously with lansoprazole for at least one year did not show evidence of ECL cell effects similar to those seen in rat studies. Longer term data are needed to rule out the possibility of an increased risk of the development of gastric tumors in patients receiving long-term therapy with lansoprazole.

Other Gastric Effects in Humans

Lansoprazole did not significantly affect mucosal blood flow in the fundus of the stomach. Due to the normal physiologic effect caused by the inhibition of gastric acid secretion, a decrease of about 17% in blood flow in the antrum, pylorus, and duodenal bulb was seen. Lansoprazole significantly slowed the gastric emptying of digestible solids. Lansoprazole increased serum pepsinogen levels and decreased pepsin activity under basal conditions and in response to meal stimulation or insulin injection. As with other agents that elevate intragastric pH, increases in gastric pH were associated with increases in nitrate-reducing bacteria and elevation of nitrite concentration in gastric juice in patients with gastric ulcer. No significant increase in nitrosamine concentrations was observed.

Serum Gastrin Effects

In over 2100 patients, median fasting serum gastrin levels increased 50% to 100% from baseline but remained within normal range after treatment with 15 to 60 mg of oral lansoprazole. These elevations reached a plateau within two months of therapy and returned to pretreatment levels within four weeks after discontinuation of therapy.

Endocrine Effects

Human studies for up to one year have not detected any clinically significant effects on the endocrine system. Hormones studied include testosterone, luteinizing hormone (LH), follicle stimulating hormone (FSH), sex hormone binding globulin (SHBG), dehydroepiandrosterone sulfate (DHEA-S), prolactin, cortisol, estradiol, insulin, aldosterone, parathormone, glucagon, thyroid stimulating hormone (TSH), triiodothyronine (T_3), thyroxine (T_4), and somatotropic hormone (STH). Lansoprazole in oral doses of 15 to 60 mg for up to one year had no clinically significant effect on sexual function. In addition, lansoprazole in oral doses of 15 to 60 mg for two to eight weeks had no clinically significant effect on thyroid function.

In 24-month carcinogenicity studies in Sprague-Dawley rats with daily lansoprazole dosages up to 150 mg/kg, proliferative changes in the Leydig cells of the testes, including benign neoplasm, were increased compared to control rates.

Other Effects

No systemic effects of lansoprazole on the central nervous system, lymphoid, hematopoietic, renal, hepatic, cardiovascular, or respiratory systems have been found in humans. Among 56 patients who had extensive baseline eye evaluations, no visual toxicity was observed after lansoprazole treatment (up to 180 mg/day) for up to 58 months.

After lifetime lansoprazole exposure in rats, focal pancreatic atrophy, diffuse lymphoid hyperplasia in the thymus, and spontaneous retinal atrophy were seen.

Microbiology
Lansoprazole, clarithromycin and/or amoxicillin have been shown to be active against most strains of *Helicobacter pylori in vitro* and in clinical infections as described in the **INDICATIONS AND USAGE** section.

Helicobacter
Helicobacter pylori

Pretreatment Resistance
Clarithromycin pretreatment resistance (≥2.0 µg/mL) was 9.5% (91/960) by E-test and 11.3% (12/106) by agar dilution in the dual and triple therapy clinical trials (M93-125, M93-130, M93-131, M95-392, and M95-399).

Amoxicillin pretreatment susceptible isolates (≤0.25 µg/mL) occurred in 97.8% (936/957) and 98.0% (98/100) of the patients in the dual and triple therapy clinical trials by E-test and agar dilution, respectively. Twenty-one of 957 patients (2.2%) by E-test and 2 of 100 patients (2.0%) by agar dilution had amoxicillin pretreatment MICs of greater than 0.25 µg/mL. One patient on the 14-day triple therapy regimen had an unconfirmed pretreatment amoxicillin minimum inhibitory concentration (MIC) of greater than 256 µg/mL by E-test and the patient was eradicated of *H. pylori* (Table 3).

Table 3: Clarithromycin Susceptibility Test Results and Clinical/Bacteriological Outcomes[a]

Clarithromycin Pretreatment Results		Clarithromycin Post-treatment Results				
		H. pylori negative – eradicated	*H. pylori* positive – not eradicated			
			Post-treatment susceptibility results			
			S[b]	I[b]	R[b]	No MIC
Triple Therapy 14-Day (lansoprazole 30 mg b.i.d./amoxicillin 1 gm b.i.d./clarithromycin 500 mg b.i.d.) (M95-399, M93-131, M95-392)						
Susceptible[b]	112	105				7
Intermediate[b]	3	3				
Resistant[b]	17	6			7	4
Triple Therapy 10-Day (lansoprazole 30 mg b.i.d./amoxicillin 1 gm b.i.d./clarithromycin 500 mg b.i.d.) (M95-399)						
Susceptible[b]	42	40	1		1	
Intermediate[b]						
Resistant[b]	4	1			3	

[a]Includes only patients with pretreatment clarithromycin susceptibility test results
[b]Susceptible (S) MIC ≤0.25 µg/mL, Intermediate (I) MIC 0.5 - 1.0 µg/mL, Resistant (R) MIC ≥2 µg/mL

Patients not eradicated of *H. pylori* following lansoprazole/amoxicillin/clarithromycin triple therapy will likely have clarithromycin resistant *H. pylori.* Therefore, for those patients who fail therapy, clarithromycin susceptibility testing should be done when possible. Patients with clarithromycin

resistant *H. pylori* should not be treated with lansoprazole/amoxicillin/clarithromycin triple therapy or with regimens which include clarithromycin as the sole antimicrobial agent.

Amoxicillin Susceptibility Test Results and Clinical/Bacteriological Outcomes

In the dual and triple therapy clinical trials, 82.6% (195/236) of the patients that had pretreatment amoxicillin susceptible MICs (≤0.25 µg/mL) were eradicated of *H. pylori*. Of those with pretreatment amoxicillin MICs of greater than 0.25 µg/mL, three of six had the *H. pylori* eradicated. A total of 30% (21/70) of the patients failed lansoprazole 30 mg t.i.d./amoxicillin 1 gm t.i.d. dual therapy and a total of 12.8% (22/172) of the patients failed the 10- and 14-day triple therapy regimens. Post-treatment susceptibility results were not obtained on 11 of the patients who failed therapy. Nine of the 11 patients with amoxicillin post-treatment MICs that failed the triple therapy regimen also had clarithromycin resistant *H. pylori* isolates.

Susceptibility Test for *Helicobacter pylori*

The reference methodology for susceptibility testing of *H. pylori* is agar dilution MICs.[1] One to three microliters of an inoculum equivalent to a No. 2 McFarland standard ($1 \times 10^7 - 1 \times 10^8$ CFU/mL for *H. pylori*) are inoculated directly onto freshly prepared antimicrobial-containing Mueller-Hinton agar plates with 5% aged defibrinated sheep blood (≥ 2 weeks old). The agar dilution plates are incubated at 35°C in a microaerobic environment produced by a gas generating system suitable for campylobacters. After 3 days of incubation, the MICs are recorded as the lowest concentration of antimicrobial agent required to inhibit growth of the organism. The clarithromycin and amoxicillin MIC values should be interpreted according to the following criteria:

Clarithromycin MIC (µg/mL)[a]	Interpretation
≤0.25	Susceptible (S)
0.5-1.0	Intermediate (I)
≥2.0	Resistant (R)

Amoxicillin MIC (µg/mL)[b]	Interpretation
≤0.25	Susceptible (S)

[a] These are tentative breakpoints for the agar dilution methodology and they should not be used to interpret results obtained using alternative methods.

[b] There were not enough organisms with MICs greater than 0.25 µg/mL to determine a resistance breakpoint.

Standardized susceptibility test procedures require the use of laboratory control microorganisms to control the technical aspects of the laboratory procedures. Standard clarithromycin and amoxicillin powders should provide the following MIC values:

Microorganism	Antimicrobial Agent	MIC (µg/mL)[a]
H. pylori ATCC 43504	Clarithromycin	0.015-0.12 µg/mL
H. pylori ATCC 43504	Amoxicillin	0.015-0.12 µg/mL

[a] These are quality control ranges for the agar dilution methodology and they should not be used to control test results obtained using alternative methods.

Reference

1. National Committee for Clinical Laboratory Standards. Summary Minutes, Subcommittee on Antimicrobial Susceptibility Testing, Tampa, FL, January 11-13, 1998.

CLINICAL STUDIES

Duodenal Ulcer

In a U.S. multicenter, double-blind, placebo-controlled, dose-response (15, 30, and 60 mg of PREVACID once daily) study of 284 patients with endoscopically documented duodenal ulcer, the percentage of patients healed after two and four weeks was significantly higher with all doses of PREVACID than with placebo. There was no evidence of a greater or earlier response with the two higher doses compared with PREVACID 15 mg. Based on this study and the second study described below, the recommended dose of PREVACID in duodenal ulcer is 15 mg per day (Table 4).

Table 4: Duodenal Ulcer Healing Rates

	PREVACID			Placebo
Week	15 mg daily (N=68)	30 mg daily (N=74)	60 mg daily (N=70)	(N=72)
2	42.4%*	35.6%*	39.1%*	11.3%
4	89.4%*	91.7%*	89.9%*	46.1%

* ($p \leq 0.001$) versus placebo.

PREVACID 15 mg was significantly more effective than placebo in relieving day and nighttime abdominal pain and in decreasing the amount of antacid taken per day.

In a second U.S. multicenter study, also double-blind, placebo-controlled, dose-comparison (15 and 30 mg of PREVACID once daily), and including a comparison with ranitidine, in 280 patients with endoscopically documented duodenal ulcer, the percentage of patients healed after four weeks was significantly higher with both doses of PREVACID than with placebo. There was no evidence of a greater or earlier response with the higher dose of PREVACID. Although the 15 mg dose of PREVACID was superior to ranitidine at 4 weeks, the lack of significant difference at 2 weeks and the absence of a difference between 30 mg of PREVACID and ranitidine leaves the comparative effectiveness of the two agents undetermined (Table 5).

Table 5: Duodenal Ulcer Healing Rates

	PREVACID		Ranitidine	Placebo
Week	15 mg daily (N=80)	30 mg daily (N=77)	300 mg h.s. (N=82)	(N=41)
2	35.0%	44.2%	30.5%	34.2%
4	92.3%**	80.3%*	70.5%*	47.5%

* ($p \leq 0.05$) versus placebo.

** ($p \leq 0.05$) versus placebo and ranitidine.

H. pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence

Randomized, double-blind clinical studies performed in the U.S. in patients with *H. pylori* and duodenal ulcer disease (defined as an active ulcer or history of an ulcer within one year) evaluated the efficacy of PREVACID in combination with amoxicillin capsules and clarithromycin tablets as triple 14-day therapy or in combination with amoxicillin capsules as dual 14-day therapy for the eradication of *H. pylori.* Based on the results of these studies, the safety and efficacy of two different eradication regimens were established:

Triple therapy:	PREVACID 30 mg b.i.d./ amoxicillin 1 gm b.i.d./ clarithromycin 500 mg b.i.d.
Dual therapy:	PREVACID 30 mg t.i.d./ amoxicillin 1 gm t.i.d.

All treatments were for 14 days. *H. pylori* eradication was defined as two negative tests (culture and histology) at 4-6 weeks following the end of treatment.

Triple therapy was shown to be more effective than all possible dual therapy combinations. Dual therapy was shown to be more effective than both monotherapies. Eradication of *H. pylori* has been shown to reduce the risk of duodenal ulcer recurrence.

A randomized, double-blind clinical study performed in the U.S. in patients with *H. pylori* and duodenal ulcer disease (defined as an active ulcer or history of an ulcer within one year) compared the efficacy of PREVACID triple therapy for 10 and 14 days. This study established that the 10-day triple therapy was equivalent to the 14-day triple therapy in eradicating *H. pylori* (Tables 6 and 7).

Table 6

***H. pylori* Eradication Rates – Triple Therapy**
(PREVACID/amoxicillin/clarithromycin)
Percent of Patients Cured
[95% Confidence Interval]
(Number of patients)

Study	Duration	Triple Therapy Evaluable Analysis*	Triple Therapy Intent-to-Treat Analysis#
M93-131	14 days	92† [80.0-97.7] (N=48)	86† [73.3-93.5] (N=55)
M95-392	14 days	86‡ [75.7-93.6] (N=66)	83‡ [72.0-90.8] (N=70)
M95-399+	14 days	85 [77.0-91.0] (N=113)	82 [73.9-88.1] (N=126)
	10 days	84 [76.0-89.8] (N=123)	81 [73.9-87.6] (N=135)

* Based on evaluable patients with confirmed duodenal ulcer (active or within one year) and *H. pylori* infection at baseline defined as at least two of three positive endoscopic tests from CLOtest®, histology and/or culture. Patients were included in the analysis if they completed the study. Additionally, if patients dropped out of the study due to an adverse event related to the study drug, they were included in the evaluable analysis as failures of therapy.

\# Patients were included in the analysis if they had documented *H. pylori* infection at baseline as defined above and had a confirmed duodenal ulcer (active or within one year). All dropouts were included as failures of therapy.

† ($p<0.05$) versus PREVACID/amoxicillin and PREVACID/clarithromycin dual therapy

‡ ($p<0.05$) versus clarithromycin/amoxicillin dual therapy

\+ The 95% confidence interval for the difference in eradication rates, 10-day minus 14-day is (-10.5, 8.1) in the evaluable analysis and (-9.7, 9.1) in the intent-to-treat analysis.

Table 7
***H. pylori* Eradication Rates – 14-Day Dual Therapy**
(PREVACID/amoxicillin)
Percent of Patients Cured
[95% Confidence Interval]
(Number of patients)

Study	Dual Therapy Evaluable Analysis*	Dual Therapy Intent-to-Treat Analysis#
M93-131	77† [62.5-87.2] (N=51)	70† [56.8-81.2] (N=60)
M93-125	66‡ [51.9-77.5] (N=58)	61‡ [48.5-72.9] (N=67)

* Based on evaluable patients with confirmed duodenal ulcer (active or within one year) and *H. pylori* infection at baseline defined as at least two of three positive endoscopic tests from CLOtest®, histology and/or culture. Patients were included in the analysis if they completed the study. Additionally, if patients dropped out of the study due to an adverse event related to the study drug, they were included in the analysis as failures of therapy.

\# Patients were included in the analysis if they had documented *H. pylori* infection at baseline as defined above and had a confirmed duodenal ulcer (active or within one year). All dropouts were included as failures of therapy.

† ($p<0.05$) versus PREVACID alone.

‡ ($p<0.05$) versus PREVACID alone or amoxicillin alone.

Long-Term Maintenance Treatment of Duodenal Ulcers

PREVACID has been shown to prevent the recurrence of duodenal ulcers. Two independent, double-blind, multicenter, controlled trials were conducted in patients with endoscopically confirmed healed duodenal ulcers. Patients remained healed significantly longer and the number of recurrences of duodenal ulcers was significantly less in patients treated with PREVACID than in patients treated with placebo over a 12-month period (Table 8).

Table 8: Endoscopic Remission Rates

Trial	Drug	No. of Pts.	Percent in Endoscopic Remission 0-3 mo.	0-6 mo.	0-12 mo.
#1	PREVACID 15 mg daily	86	90%*	87%*	84%*
	Placebo	83	49%	41%	39%
#2	PREVACID 30 mg daily	18	94%*	94%*	85%*
	PREVACID 15 mg daily	15	87%*	79%*	70%*
	Placebo	15	33%	0%	0%

%=Life Table Estimate

* ($p\leq0.001$) versus placebo.

In trial #2, no significant difference was noted between PREVACID 15 mg and 30 mg in maintaining remission.

Gastric Ulcer

In a U.S. multicenter, double-blind, placebo-controlled study of 253 patients with endoscopically documented gastric ulcer, the percentage of patients healed at four and eight weeks was significantly higher with PREVACID 15 mg and 30 mg once a day than with placebo (Table 9).

Table 9: Gastric Ulcer Healing Rates

	PREVACID			Placebo
Week	15 mg daily (N=65)	30 mg daily (N=63)	60 mg daily (N=61)	(N=64)
4	64.6%*	58.1%*	53.3%*	37.5%
8	92.2%*	96.8%*	93.2%*	76.7%

* ($p \leq 0.05$) versus placebo.

Patients treated with any PREVACID dose reported significantly less day and night abdominal pain along with fewer days of antacid use and fewer antacid tablets used per day than the placebo group.

Independent substantiation of the effectiveness of PREVACID 30 mg was provided by a meta-analysis of published and unpublished data.

Healing of NSAID-Associated Gastric Ulcer

IN TWO U.S. AND CANADIAN MULTICENTER, DOUBLE-BLIND, ACTIVE-CONTROLLED STUDIES IN PATIENTS WITH ENDOSCOPICALLY CONFIRMED NSAID-ASSOCIATED GASTRIC ULCER WHO CONTINUED THEIR NSAID USE, THE PERCENTAGE OF PATIENTS HEALED AFTER 8 WEEKS WAS STATISTICALLY SIGNIFICANTLY HIGHER WITH 30 MG OF PREVACID THAN WITH THE ACTIVE CONTROL. A TOTAL OF 711 PATIENTS WERE ENROLLED IN THE STUDY, AND 701 PATIENTS WERE TREATED. PATIENTS RANGED IN AGE FROM 18 TO 88 YEARS (MEDIAN AGE 59 YEARS), WITH 67% FEMALE PATIENTS AND 33% MALE PATIENTS. RACE WAS DISTRIBUTED AS FOLLOWS: 87% CAUCASIAN, 8% BLACK, 5% OTHER. THERE WAS NO STATISTICALLY SIGNIFICANT DIFFERENCE BETWEEN PREVACID 30 MG DAILY AND THE ACTIVE CONTROL ON SYMPTOM RELIEF (I.E., ABDOMINAL PAIN) (TABLE 10).

Table 10: NSAID-Associated Gastric Ulcer Healing Rates [1]

	Study #1	
	PREVACID 30 mg daily	Active Control [2]
Week 4	60% (53/88) [3]	28% (23/83)
Week 8	79% (62/79) [3]	55% (41/74)
	Study #2	
	PREVACID 30 mg daily	Active Control [2]
Week 4	53% (40/75)	38% (31/82)
Week 8	77% (47/61) [3]	50% (33/66)

[1] Actual observed ulcer(s) healed at time points $\pm$ 2 days

[2] Dose for healing of gastric ulcer

[3] ($p \leq 0.05$) versus the active control

Risk Reduction of NSAID-Associated Gastric Ulcer

IN ONE LARGE U.S., MULTICENTER, DOUBLE-BLIND, PLACEBO- AND MISOPROSTOL-CONTROLLED (MISOPROSTOL BLINDED ONLY TO THE ENDOSCOPIST) STUDY IN PATIENTS WHO REQUIRED CHRONIC USE OF AN NSAID AND WHO HAD A HISTORY OF AN ENDOSCOPICALLY DOCUMENTED GASTRIC ULCER, THE PROPORTION OF PATIENTS REMAINING FREE FROM GASTRIC ULCER AT 4, 8, AND 12 WEEKS WAS SIGNIFICANTLY HIGHER WITH 15 OR 30 MG OF PREVACID THAN PLACEBO. A TOTAL OF 537 PATIENTS WERE ENROLLED IN THE STUDY, AND 535 PATIENTS WERE TREATED. PATIENTS RANGED IN AGE FROM 23 TO 89 YEARS (MEDIAN AGE 60 YEARS), WITH 65% FEMALE PATIENTS AND 35% MALE PATIENTS. RACE WAS DISTRIBUTED AS FOLLOWS: 90% CAUCASIAN, 6% BLACK, 4% OTHER. THE 30 MG DOSE OF PREVACID DEMONSTRATED NO ADDITIONAL BENEFIT IN RISK REDUCTION OF THE NSAID-ASSOCIATED GASTRIC ULCER THAN THE 15 MG DOSE (TABLE 11).

Table 11: Proportion of Patients Remaining Free of Gastric Ulcers[1]

Week	PREVACID 15 mg daily (N=121)	PREVACID 30 mg daily (N=116)	Misoprostol 200 µg q.i.d. (N=106)	Placebo (N=112)
4	90%	92%	96%	66%
8	86%	88%	95%	60%
12	80%	82%	93%	51%

[1] % = Life Table Estimate

($p<0.001$) PREVACID 15 mg daily versus placebo; PREVACID 30 mg daily versus placebo; and misoprostol 200 µg q.i.d. versus placebo.

($p<0.05$) Misoprostol 200 µg q.i.d. versus PREVACID 15 mg daily; and misoprostol 200 µg q.i.d. versus PREVACID 30 mg daily

Gastroesophageal Reflux Disease (GERD)

Symptomatic GERD

In a U.S. multicenter, double-blind, placebo-controlled study of 214 patients with frequent GERD symptoms, but no esophageal erosions by endoscopy, significantly greater relief of heartburn associated with GERD was observed with the administration of lansoprazole 15 mg once daily up to 8 weeks than with placebo. No significant additional benefit from lansoprazole 30 mg once daily was observed.

The intent-to-treat analyses demonstrated significant reduction in frequency and severity of day and night heartburn. Data for frequency and severity for the 8-week treatment period are presented in Table 12 and in Figures 1 and 2:

Table 12: Frequency of Heartburn

Variable	Placebo (n=43)	PREVACID 15 mg (n=80)	PREVACID 30 mg (n=86)
		Median	
% of Days without Heartburn			
Week 1	0%	71%*	46%*
Week 4	11%	81%*	76%*
Week 8	13%	84%*	82%*
% of Nights without Heartburn			
Week 1	17%	86%*	57%*
Week 4	25%	89%*	73%*
Week 8	36%	92%*	80%*

* ($p<0.01$) versus placebo.

Figure 1

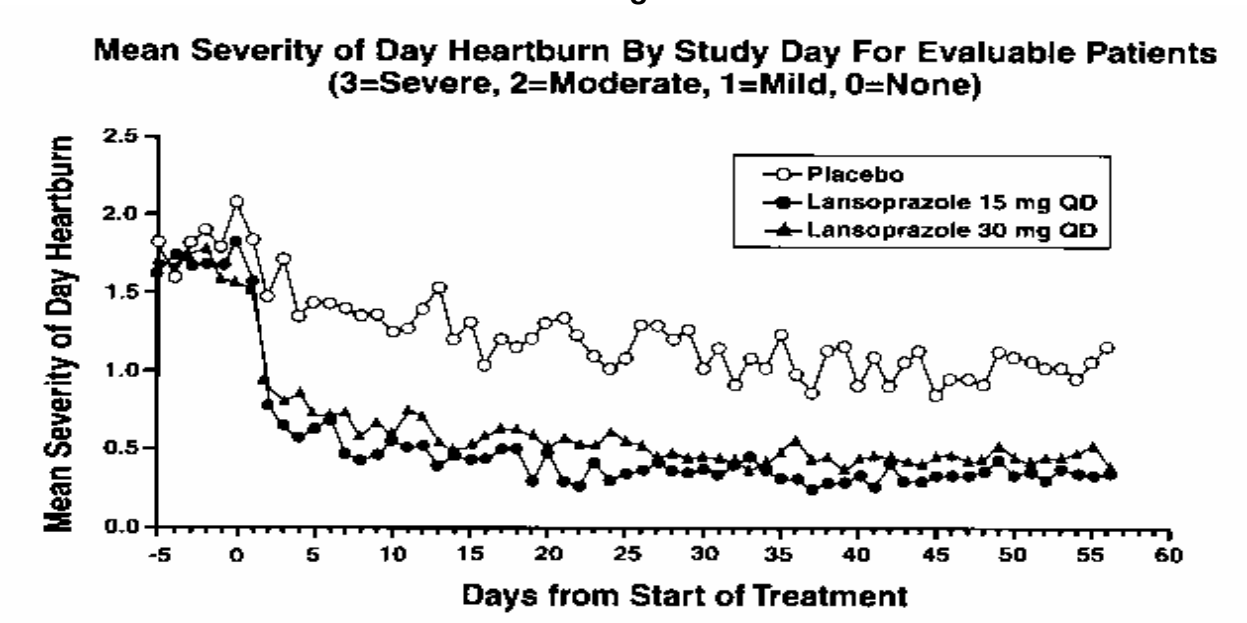
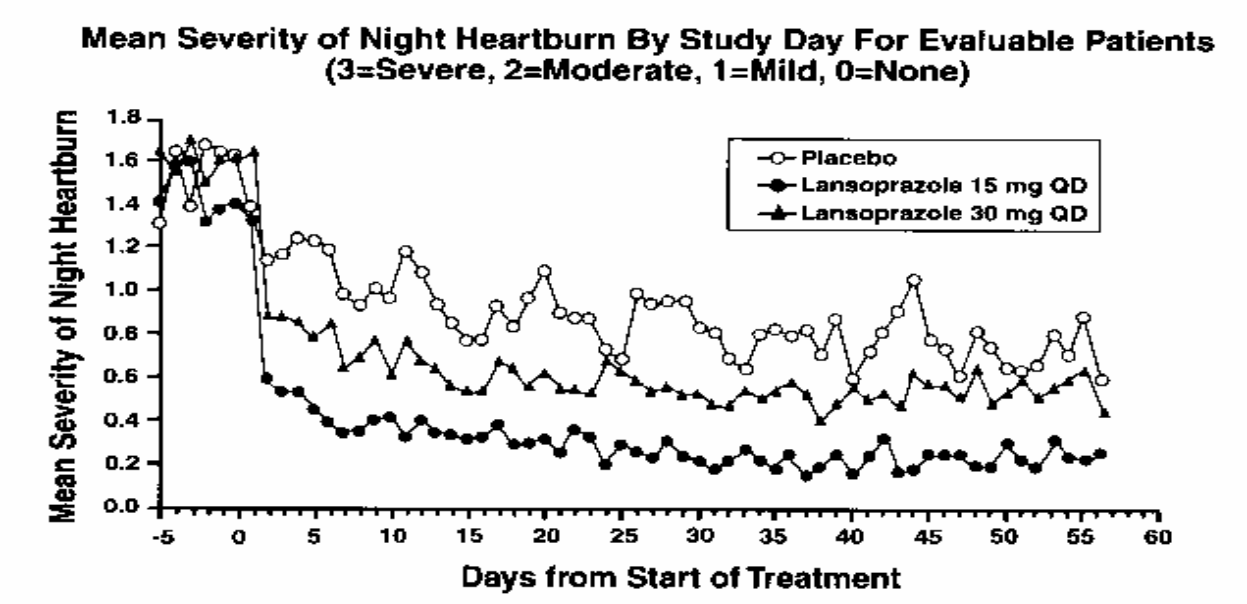


Figure 2



In two U.S., multicenter double-blind, ranitidine-controlled studies of 925 total patients with frequent GERD symptoms, but no esophageal erosions by endoscopy, lansoprazole 15 mg was superior to ranitidine 150 mg (b.i.d.) in decreasing the frequency and severity of day and night heartburn associated with GERD for the 8-week treatment period. No significant additional benefit from lansoprazole 30 mg once daily was observed.

Erosive Esophagitis

In a U.S. multicenter, double-blind, placebo-controlled study of 269 patients entering with an endoscopic diagnosis of esophagitis with mucosal grading of 2 or more and grades 3 and 4 signifying erosive disease, the percentages of patients with healing are presented in Table 13:

Table 13: Erosive Esophagitis Healing Rates

	PREVACID			Placebo
Week	15 mg daily (N=69)	30 mg daily (N=65)	60 mg daily (N=72)	(N=63)
4	67.6%*	81.3%*†	80.6%*†	32.8%
6	87.7%*	95.4%*	94.3%*	52.5%
8	90.9%*	95.4%*	94.4%*	52.5%

* ($p \leq 0.001$) versus placebo.
† ($p \leq 0.05$) versus PREVACID 15 mg.

In this study, all PREVACID groups reported significantly greater relief of heartburn and less day and night abdominal pain along with fewer days of antacid use and fewer antacid tablets taken per day than the placebo group.

Although all doses were effective, the earlier healing in the higher two doses suggests 30 mg daily as the recommended dose.

PREVACID was also compared in a U.S. multicenter, double-blind study to a low dose of ranitidine in 242 patients with erosive reflux esophagitis. PREVACID at a dose of 30 mg was significantly more effective than ranitidine 150 mg b.i.d. as shown below (Table 14).

Table 14: Erosive Esophagitis Healing Rates

Week	PREVACID 30 mg daily (N=115)	Ranitidine 150 mg b.i.d. (N=127)
2	66.7%*	38.7%
4	82.5%*	52.0%
6	93.0%*	67.8%
8	92.1%*	69.9%

* ($p \leq 0.001$) versus ranitidine.

In addition, patients treated with PREVACID reported less day and nighttime heartburn and took less antacid tablets for fewer days than patients taking ranitidine 150 mg b.i.d.

Although this study demonstrates effectiveness of PREVACID in healing erosive esophagitis, it does not represent an adequate comparison with ranitidine because the recommended ranitidine dose for esophagitis is 150 mg q.i.d., twice the dose used in this study.

In the two trials described and in several smaller studies involving patients with moderate to severe erosive esophagitis, PREVACID produced healing rates similar to those shown above.

In a U.S. multicenter, double-blind, active-controlled study, 30 mg of PREVACID was compared with ranitidine 150 mg b.i.d. in 151 patients with erosive reflux esophagitis that was poorly responsive

to a minimum of 12 weeks of treatment with at least one H_2-receptor antagonist given at the dose indicated for symptom relief or greater, namely, cimetidine 800 mg/day, ranitidine 300 mg/day, famotidine 40 mg/day or nizatidine 300 mg/day. PREVACID 30 mg was more effective than ranitidine 150 mg b.i.d. in healing reflux esophagitis, and the percentage of patients with healing were as follows. This study does not constitute a comparison of the effectiveness of histamine H_2-receptor antagonists with PREVACID, as all patients had demonstrated unresponsiveness to the histamine H_2-receptor antagonist mode of treatment. It does indicate, however, that PREVACID may be useful in patients failing on a histamine H_2-receptor antagonist (Table 15).

Table 15: Reflux Esophagitis Healing Rates in Patients Poorly Responsive to Histamine H_2-Receptor Antagonist Therapy

Week	PREVACID 30 mg daily (N=100)	Ranitidine 150 mg b.i.d. (N=51)
4	74.7%*	42.6%
8	83.7%*	32.0%

* ($p \leq 0.001$) versus ranitidine.

Long-Term Maintenance Treatment of Erosive Esophagitis

Two independent, double-blind, multicenter, controlled trials were conducted in patients with endoscopically confirmed healed esophagitis. Patients remained in remission significantly longer and the number of recurrences of erosive esophagitis was significantly less in patients treated with PREVACID than in patients treated with placebo over a 12-month period (Table 16).

Table 16: Endoscopic Remission Rates

			Percent in Endoscopic Remission		
Trial	Drug	No. of Pts.	0-3 mo.	0-6 mo.	0-12 mo.
#1	PREVACID 15 mg daily	59	83%*	81%*	79%*
	PREVACID 30 mg daily	56	93%*	93%*	90%*
	Placebo	55	31%	27%	24%
#2	PREVACID 15 mg daily	50	74%*	72%*	67%*
	PREVACID 30 mg daily	49	75%*	72%*	55%*
	Placebo	47	16%	13%	13%

%=Life Table Estimate
* ($p \leq 0.001$) versus placebo.

Regardless of initial grade of erosive esophagitis, PREVACID 15 mg and 30 mg were similar in maintaining remission.

In a U.S., randomized, double-blind, study, PREVACID 15 mg daily (n = 100) was compared with ranitidine 150 mg b.i.d. (n = 106), at the recommended dosage, in patients with endoscopically-proven healed erosive esophagitis over a 12-month period. Treatment with PREVACID resulted in patients remaining healed (Grade 0 lesions) of erosive esophagitis for significantly longer periods of time than

those treated with ranitidine ($p<0.001$). In addition, PREVACID was significantly more effective than ranitidine in providing complete relief of both daytime and nighttime heartburn. Patients treated with PREVACID remained asymptomatic for a significantly longer period of time than patients treated with ranitidine.

Pathological Hypersecretory Conditions Including Zollinger-Ellison Syndrome

In open studies of 57 patients with pathological hypersecretory conditions, such as Zollinger-Ellison (ZE) syndrome with or without multiple endocrine adenomas, PREVACID significantly inhibited gastric acid secretion and controlled associated symptoms of diarrhea, anorexia and pain. Doses ranging from 15 mg every other day to 180 mg per day maintained basal acid secretion below 10 mEq/hr in patients without prior gastric surgery and below 5 mEq/hr in patients with prior gastric surgery.

Initial doses were titrated to the individual patient need, and adjustments were necessary with time in some patients (see **DOSAGE AND ADMINISTRATION**). PREVACID was well tolerated at these high dose levels for prolonged periods (greater than four years in some patients). In most ZE patients, serum gastrin levels were not modified by PREVACID. However, in some patients, serum gastrin increased to levels greater than those present prior to initiation of lansoprazole therapy.

INDICATIONS AND USAGE

PREVACID Delayed-Release Capsules, PREVACID SoluTab Delayed-Release Orally Disintegrating Tablets and PREVACID For Delayed-Release Oral Suspension are indicated for:

Short-Term Treatment of Active Duodenal Ulcer

PREVACID is indicated for short-term treatment (for 4 weeks) for healing and symptom relief of active duodenal ulcer.

H. pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence

Triple Therapy: PREVACID/amoxicillin/clarithromycin

PREVACID in combination with amoxicillin plus clarithromycin as triple therapy is indicated for the treatment of patients with *H. pylori* infection and duodenal ulcer disease (active or one-year history of a duodenal ulcer) to eradicate *H. pylori*. Eradication of *H. pylori* has been shown to reduce the risk of duodenal ulcer recurrence (see **CLINICAL STUDIES** and **DOSAGE AND ADMINISTRATION**).

Dual Therapy: PREVACID/amoxicillin

PREVACID in combination with amoxicillin as dual therapy is indicated for the treatment of patients with *H. pylori* infection and duodenal ulcer disease (active or one-year history of a duodenal ulcer) **who are either allergic or intolerant to clarithromycin or in whom resistance to clarithromycin is known or suspected** (see the clarithromycin package insert, **MICROBIOLOGY** section). Eradication of *H. pylori* has been shown to reduce the risk of duodenal ulcer recurrence (see **CLINICAL STUDIES** and **DOSAGE AND ADMINISTRATION**).

Maintenance of Healed Duodenal Ulcers

PREVACID is indicated to maintain healing of duodenal ulcers. Controlled studies do not extend beyond 12 months.

Short-Term Treatment of Active Benign Gastric Ulcer
PREVACID is indicated for short-term treatment (up to 8 weeks) for healing and symptom relief of active benign gastric ulcer.

Healing of NSAID-Associated Gastric Ulcer
PREVACID is indicated for the treatment of NSAID-associated gastric ulcer in patients who continue NSAID use. Controlled studies did not extend beyond 8 weeks.

Risk Reduction of NSAID-Associated Gastric Ulcer
PREVACID is indicated for reducing the risk of NSAID-associated gastric ulcers in patients with a history of a documented gastric ulcer who require the use of an NSAID. Controlled studies did not extend beyond 12 weeks.

Gastroesophageal Reflux Disease (GERD)
Short-Term Treatment of Symptomatic GERD
PREVACID is indicated for the treatment of heartburn and other symptoms associated with GERD.

Short-Term Treatment of Erosive Esophagitis
PREVACID is indicated for short-term treatment (up to 8 weeks) for healing and symptom relief of all grades of erosive esophagitis.

For patients who do not heal with PREVACID for 8 weeks (5-10%), it may be helpful to give an additional 8 weeks of treatment.

If there is a recurrence of erosive esophagitis an additional 8-week course of PREVACID may be considered.

Maintenance of Healing of Erosive Esophagitis
PREVACID is indicated to maintain healing of erosive esophagitis. Controlled studies did not extend beyond 12 months.

Pathological Hypersecretory Conditions Including Zollinger-Ellison Syndrome
PREVACID is indicated for the long-term treatment of pathological hypersecretory conditions, including Zollinger-Ellison syndrome.

CONTRAINDICATIONS
PREVACID is contraindicated in patients with known severe hypersensitivity to any component of the formulation of PREVACID.

Amoxicillin is contraindicated in patients with a known hypersensitivity to any penicillin.

Clarithromycin is contraindicated in patients with a known hypersensitivity to clarithromycin, erythromycin, and any of the macrolide antibiotics.

Concomitant administration of clarithromycin and any of the following drugs is contraindicated: cisapride, pimozide, astemizole, terfenadine, ergotamine or dihydroergotamine. There have been post-marketing reports of drug interactions when clarithromycin and/or erythromycin are co-administered with cisapride, pimozide, astemizole, or terfenadine resulting in cardiac arrhythmias (QT prolongation,

ventricular tachycardia, ventricular fibrillation, and torsades de pointes) most likely due to inhibition of metabolism of these drugs by erythromycin and clarithromycin. Fatalities have been reported.

For information about contraindications of other drugs that may be used in combination with amoxicillin or clarithromycin, refer to the **CONTRAINDICATIONS** section of their package inserts.

Please refer to full prescribing information for amoxicillin and clarithromycin before prescribing.

WARNINGS

CLARITHROMYCIN SHOULD NOT BE USED IN PREGNANT WOMEN EXCEPT IN CLINICAL CIRCUMSTANCES WHERE NO ALTERNATIVE THERAPY IS APPROPRIATE. IF PREGNANCY OCCURS WHILE TAKING CLARITHROMYCIN, THE PATIENT SHOULD BE APPRISED OF THE POTENTIAL HAZARD TO THE FETUS (see **WARNINGS** in the prescribing information for clarithromycin).

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including clarithromycin and amoxicillin, and may range in severity from mild to life threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.

Treatment with antibacterial agents alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is a primary cause of "antibiotic-associated colitis."

After the diagnosis of pseudomembranous colitis has been established, therapeutic measures should be initiated. Mild cases of pseudomembranous colitis usually respond to discontinuation of the drug alone. In moderate to severe cases, consideration should be given to management with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against *Clostridium difficile* colitis.

There have been post-marketing reports of colchicine toxicity with concomitant use of clarithromycin and colchicine, especially in the elderly, some of which occurred in patients with renal insufficiency. Deaths have been reported in some such patients.

Serious and occasionally fatal hypersensitivity (anaphylactic) reactions have been reported in patients on penicillin therapy. These reactions are more apt to occur in individuals with a history of penicillin hypersensitivity and/or a history of sensitivity to multiple allergens.

There have been well-documented reports of individuals with a history of penicillin hypersensitivity reactions who have experienced severe hypersensitivity reactions when treated with a cephalosporin. Before initiating therapy with any penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, and other allergens. If an allergic reaction occurs, amoxicillin should be discontinued and the appropriate therapy instituted.

SERIOUS ANAPHYLACTIC REACTIONS REQUIRE IMMEDIATE EMERGENCY TREATMENT WITH EPINEPHRINE. OXYGEN, INTRAVENOUS STEROIDS, AND AIRWAY MANAGEMENT, INCLUDING INTUBATION, SHOULD ALSO BE ADMINISTERED AS INDICATED.

For information about warnings of other drugs that may be used in combination with amoxicillin or clarithromycin, refer to the **WARNINGS** section of their package inserts.

PRECAUTIONS

General

Symptomatic response to therapy with lansoprazole does not preclude the presence of gastric malignancy.

For information about precautions of other drugs that may be used in combination with amoxicillin or clarithromycin, refer to the **PRECAUTIONS** section of their package inserts.

Information for Patients

PREVACID is available as a capsule, orally disintegrating tablet and oral suspension, and is available in 15 mg and 30 mg strengths. Directions for use specific to the route and available methods of administration for each of these dosage forms is presented below. PREVACID should be taken before eating. PREVACID products SHOULD NOT BE CRUSHED OR CHEWED.

Phenylketonurics: Contains Phenylalanine 2.5 mg per 15 mg Tablet and 5.1 mg per 30 mg Tablet.

Administration Options

1. *PREVACID Delayed-Release Capsules*

PREVACID Delayed-Release Capsules should be swallowed whole.

Alternatively, for patients who have difficulty swallowing capsules, PREVACID Delayed-Release Capsules can be opened and administered as follows:

- Open capsule.
- Sprinkle intact granules on one tablespoon of either applesauce, ENSURE® pudding, cottage cheese, yogurt or strained pears.
- Swallow immediately.

PREVACID Delayed-Release Capsules may also be emptied into a small volume of either apple juice, orange juice or tomato juice and administered as follows:

- Open capsule.
- Sprinkle intact granules into a small volume of either apple juice, orange juice or tomato juice (60 mL – approximately 2 ounces).
- Mix briefly.
- Swallow immediately.
- To ensure complete delivery of the dose, the glass should be rinsed with two or more volumes of juice and the contents swallowed immediately.

USE IN OTHER FOODS AND LIQUIDS HAS NOT BEEN STUDIED CLINICALLY AND IS THEREFORE NOT RECOMMENDED.

2. PREVACID SoluTab Delayed-Release Orally Disintegrating Tablets

PREVACID SoluTab should not be chewed. Place the tablet on the tongue and allow it to disintegrate, with or without water, until the particles can be swallowed. The tablet typically disintegrates in less than 1 minute.

Alternatively, for children or other patients who have difficulty swallowing tablets, PREVACID SoluTab can be delivered in two different ways.

PREVACID SoluTab – Oral Syringe

For administration via oral syringe, PREVACID SoluTab can be administered as follows:

- Place a 15 mg tablet in oral syringe and draw up approximately 4 mL of water, or place a 30 mg tablet in oral syringe and draw up approximately 10 mL of water.
- Shake gently to allow for a quick dispersal.
- After the tablet has dispersed, administer the contents within 15 minutes.
- Refill the syringe with approximately 2 mL (5 mL for the 30 mg tablet) of water, shake gently, and administer any remaining contents.

PREVACID SoluTab – Nasogastric Tube Administration (≥ 8 French)

For administration via a nasogastric tube, PREVACID SoluTab can be administered as follows:

- Place a 15 mg tablet in a syringe and draw up 4 mL of water, or place a 30 mg tablet in a syringe and draw up 10 mL of water.
- Shake gently to allow for a quick dispersal.
- After the tablet has dispersed, inject through the nasogastric tube into the stomach within 15 minutes.
- Refill the syringe with approximately 5 mL of water, shake gently, and flush the nasogastric tube.

3. PREVACID for Delayed-Release Oral Suspension

PREVACID for Delayed-Release Oral Suspension should be administered as follows:

- Open packet.
- To prepare a dose, empty the packet contents into a container containing 2 tablespoons of **WATER**. DO NOT USE OTHER LIQUIDS OR FOODS.
- Stir well, and drink immediately.
- If any material remains after drinking, add more water, stir, and drink immediately.

- **This product should not be given through enteral administration tubes.**

Drug Interactions

Lansoprazole is metabolized through the cytochrome P_{450} system, specifically through the CYP3A and CYP2C19 isozymes. Studies have shown that lansoprazole does not have clinically significant interactions with other drugs metabolized by the cytochrome P_{450} system, such as warfarin, antipyrine, indomethacin, ibuprofen, phenytoin, propranolol, prednisone, diazepam, or clarithromycin in healthy subjects. These compounds are metabolized through various cytochrome P_{450} isozymes including CYP1A2, CYP2C9, CYP2C19, CYP2D6, and CYP3A. When lansoprazole was administered concomitantly with theophylline (CYP1A2, CYP3A), a minor increase (10%) in the clearance of theophylline was seen. Because of the small magnitude and the direction of the effect on theophylline clearance, this interaction is unlikely to be of clinical concern. Nonetheless, individual patients may require additional titration of their theophylline dosage when lansoprazole is started or stopped to ensure clinically effective blood levels.

In a study of healthy subjects neither the pharmacokinetics of warfarin enantiomers nor prothrombin time were affected following single or multiple 60 mg doses of lansoprazole. However, there have been reports of increased International Normalized Ratio (INR) and prothrombin time in patients receiving proton pump inhibitors, including lansoprazole, and warfarin concomitantly. Increases in INR and prothrombin time may lead to abnormal bleeding and even death. Patients treated with proton pump inhibitors and warfarin concomitantly may need to be monitored for increases in INR and prothrombin time.

In an open-label, single-arm, eight-day, pharmacokinetic study of 28 adult rheumatoid arthritis patients (who required the chronic use of 7.5 to 15 mg of methotrexate given weekly), administration of 7 days of naproxen 500 mg BID and lansoprazole 30 mg daily had no effect on the pharmacokinetics of methotrexate and 7-hydroxymethotrexate. While this study was not designed to assess the safety of this combination of drugs, no major adverse events were noted.

Lansoprazole has also been shown to have no clinically significant interaction with amoxicillin.

In a single-dose crossover study examining lansoprazole 30 mg and omeprazole 20 mg each administered alone and concomitantly with sucralfate 1 gram, absorption of the proton pump inhibitors was delayed and their bioavailability was reduced by 17% and 16%, respectively, when administered concomitantly with sucralfate. Therefore, proton pump inhibitors should be taken at least 30 minutes prior to sucralfate. In clinical trials, antacids were administered concomitantly with PREVACID and there was no evidence of a change in the efficacy of PREVACID.

Lansoprazole causes a profound and long-lasting inhibition of gastric acid secretion; therefore, it is theoretically possible that lansoprazole may interfere with the absorption of drugs where gastric pH is an important determinant of bioavailability (e.g., ketoconazole, ampicillin esters, iron salts, digoxin).

Carcinogenesis, Mutagenesis, Impairment of Fertility

In two 24-month carcinogenicity studies, Sprague-Dawley rats were treated with oral lansoprazole doses of 5 to 150 mg/kg/day - about 1 to 40 times the exposure on a body surface (mg/m^2) basis, of a 50-kg person of average height [1.46 m^2 body surface area (BSA)] given the recommended human dose of 30 mg/day (22.2 mg/m^2). Lansoprazole produced dose-related gastric enterochromaffin-like (ECL) cell hyperplasia and ECL cell carcinoids in both male and female rats. It also increased the incidence of intestinal metaplasia of the gastric epithelium in both sexes. In male rats, lansoprazole

produced a dose-related increase of testicular interstitial cell adenomas. The incidence of these adenomas in rats receiving doses of 15 to 150 mg/kg/day (4 to 40 times the recommended human dose based on BSA) exceeded the low background incidence (range = 1.4 to 10%) for this strain of rat. In addition, in a one-year toxicity study, testicular interstitial cell adenoma occurred in 1 of 30 rats treated with 50 mg/kg/day of lansoprazole (13 times the recommended human dose based on BSA).

In a 24-month carcinogenicity study, CD-1 mice were treated with oral lansoprazole doses of 15 to 600 mg/kg/day, 2 to 80 times the recommended human dose based on BSA. Lansoprazole produced a dose-related increased incidence of gastric ECL cell hyperplasia. It also produced an increased incidence of liver tumors (hepatocellular adenoma plus carcinoma). The tumor incidences in male mice treated with 300 and 600 mg/kg/day (40 to 80 times the recommended human dose based on BSA) and female mice treated with 150 to 600 mg/kg/day (20 to 80 times the recommended human dose based on BSA) exceeded the ranges of background incidences in historical controls for this strain of mice. Lansoprazole treatment produced adenoma of rete testis in male mice receiving 75 to 600 mg/kg/day (10 to 80 times the recommended human dose based on BSA).

Lansoprazole was not genotoxic in the Ames test, the *ex vivo* rat hepatocyte unscheduled DNA synthesis (UDS) test, the *in vivo* mouse micronucleus test, or the rat bone marrow cell chromosomal aberration test. It was positive in *in vitro* human lymphocyte chromosomal aberration assays.

Lansoprazole at oral doses up to 150 mg/kg/day (40 times the recommended human dose based on BSA) was found to have no effect on fertility and reproductive performance of male and female rats.

Pregnancy: Teratogenic Effects.

Pregnancy Category B

Lansoprazole

Teratology studies have been performed in pregnant rats at oral lansoprazole doses up to 150 mg/kg/day (40 times the recommended human dose based on BSA) and pregnant rabbits at oral lansoprazole doses up to 30 mg/kg/day (16 times the recommended human dose based on BSA) and have revealed no evidence of impaired fertility or harm to the fetus due to lansoprazole.

There are, however, no adequate or well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Pregnancy Category C

Clarithromycin

See **WARNINGS** (above) and full prescribing information for clarithromycin before using in pregnant women.

Nursing Mothers

Lansoprazole or its metabolites are excreted in the milk of rats. It is not known whether lansoprazole is excreted in human milk. Because many drugs are excreted in human milk, because of the potential for serious adverse reactions in nursing infants from lansoprazole, and because of the potential for tumorigenicity shown for lansoprazole in rat carcinogenicity studies, a decision should be made whether to discontinue nursing or to discontinue lansoprazole, taking into account the importance of lansoprazole to the mother.

Pediatric Use

The safety and effectiveness of PREVACID have been established in pediatric patients 1 to 17 years of age for short-term treatment of symptomatic GERD and erosive esophagitis. Use of PREVACID in this population is supported by evidence from adequate and well-controlled studies of PREVACID in adults with additional clinical, pharmacokinetic, and pharmacodynamic studies performed in pediatric patients. The adverse events profile in pediatric patients is similar to that of adults. There were no adverse events reported in U.S. clinical studies that were not previously observed in adults. The safety and effectiveness of PREVACID in patients less than 1 year of age have not been established.

1 to 11 years of age

In an uncontrolled, open-label, U.S. multicenter study, 66 pediatric patients (1 to 11 years of age) with GERD were assigned, based on body weight, to receive an initial dose of either PREVACID 15 mg daily if ≤ 30 kg or PREVACID 30 mg daily if greater than 30 kg administered for 8 to 12 weeks. The PREVACID dose was increased (up to 30 mg b.i.d.) in 24 of 66 pediatric patients after 2 or more weeks of treatment if they remained symptomatic. At baseline 85% of patients had mild to moderate overall GERD symptoms (assessed by investigator interview), 58% had non-erosive GERD and 42% had erosive esophagitis (assessed by endoscopy).

After 8 to 12 weeks of PREVACID treatment, the intent-to-treat analysis demonstrated an approximate 50% reduction in frequency and severity of GERD symptoms.

Twenty-one of 27 erosive esophagitis patients were healed at 8 weeks and 100% of patients were healed at 12 weeks by endoscopy (Table 17).

Table 17: GERD symptom improvement and Erosive Esophagitis healing rates in pediatric patients age 1 to 11

GERD	Final Visit[a] % (n/N)
Symptomatic GERD Improvement in Overall GERD Symptoms[b]	76% (47/62 [c])
Erosive Esophagitis Improvement in Overall GERD Symptoms[b] Healing Rate	81% (22/27) 100% (27/27)

[a] At Week 8 or Week 12
[b] Symptoms assessed by patients diary kept by caregiver.
[c] No data were available for 4 pediatric patients.

In a study of 66 pediatric patients in the age group 1 year to 11 years old after treatment with PREVACID given orally in doses of 15 mg daily to 30 mg b.i.d., increases in serum gastrin levels were similar to those observed in adult studies. Median fasting serum gastrin levels increased 89% from 51 pg/ mL at baseline to 97 pg/mL [interquartile range (25^{th}-75^{th} percentile) of 71-130 pg/ mL] at the final visit.

The pediatric safety of PREVACID Delayed-Release Capsules has been assessed in 66 pediatric patients aged 1 to 11 years of age. Of the 66 patients with GERD 85% (56/66) took PREVACID for 8 weeks and 15% (10/66) took it for 12 weeks.

The most frequently reported (2 or more patients) treatment-related adverse events in patients 1 to 11 years of age (N=66) were constipation (5%) and headache (3%).

12 to 17 years of age

In an uncontrolled, open-label, U.S. multicenter study, 87 adolescent patients (12 to 17 years of age) with symptomatic GERD were treated with PREVACID for 8 to 12 weeks. Baseline upper endoscopies classified these patients into two groups: 64 (74%) nonerosive GERD and 23 (26%) erosive esophagitis (EE). The nonerosive GERD patients received PREVACID 15 mg daily for 8 weeks and the EE patients received PREVACID 30 mg daily for 8 to 12 weeks. At baseline, 89% of these patients had mild to moderate overall GERD symptoms (assessed by investigator interviews). During 8 weeks of PREVACID treatment, adolescent patients experienced a 63% reduction in frequency and a 69% reduction in severity of GERD symptoms based on diary results.

Twenty-one of 22 (95.5%) adolescent erosive esophagitis patients were healed after 8 weeks of PREVACID treatment. One patient remained unhealed after 12 weeks of treatment (Table 18).

Table 18: GERD symptom improvement and Erosive Esophagitis healing rates in pediatric patients age 12 to 17

GERD	**Final Visit** % (n/N)
Symptomatic GERD (All Patients) Improvement in Overall GERD Symptoms[a]	73.2% (60/82)[b]
Nonerosive GERD Improvement in Overall GERD Symptoms[a]	71.2% (42/59)[b]
Erosive Esophagitis Improvement in Overall GERD Symptoms[a] Healing Rate[c]	78.3% (18/23) 95.5% (21/22)[c]

[a]Symptoms assessed by patient diary (parents/caregivers as necessary).
[b]No data available for 5 patients.
[c]Data from one healed patient was excluded from this analysis due to timing of final endoscopy.

In these 87 adolescent patients, increases in serum gastrin levels were similar to those observed in adult studies, median fasting serum gastrin levels increased 42% from 45 pg/mL at baseline to 64 pg/mL [interquartile range (25^{th} – 75^{th} percentile) of 44 – 88 pg/mL] at the final visit. (Normal serum gastrin levels are 25 to 111 pg/mL.)

THE SAFETY OF PREVACID DELAYED-RELEASE CAPSULES HAS BEEN ASSESSED IN THESE 87 ADOLESCENT PATIENTS. OF THE 87 ADOLESCENT PATIENTS WITH GERD, 6% (5/87) TOOK PREVACID FOR LESS THAN 6 WEEKS, 93% (81/87) FOR 6-10 WEEKS, AND 1% (1/87) FOR GREATER THAN 10 WEEKS.

The most frequently reported (at least 3%) treatment-related adverse events in these patients were headache (7%), abdominal pain (5%), nausea (3%) and dizziness (3%). Treatment-related dizziness, reported in this package insert as occurring in less than 1% of adult patients, was reported in this study by 3 adolescent patients with nonerosive GERD, who had dizziness concurrently with other events (such as migraine, dyspnea, and vomiting).

Use in Women
Over 4,000 women were treated with PREVACID. Ulcer healing rates in females were similar to those in males. The incidence rates of adverse events in females were similar to those seen in males.

Use in Geriatric Patients
The incidence rates of PREVACID-associated adverse events and laboratory test abnormalities are similar to those seen in younger patients. For geriatric patients, dosage and administration of PREVACID need not be altered.

ADVERSE REACTIONS

Clinical
Worldwide, over 10,000 patients have been treated with PREVACID in Phase 2 or Phase 3 clinical trials involving various dosages and durations of treatment. The adverse reaction profiles for PREVACID Delayed-Release Capsules and PREVACID for Delayed-Release Oral Suspension are similar. In general, PREVACID treatment has been well-tolerated in both short-term and long-term trials.

The following adverse events were reported by the treating physician to have a possible or probable relationship to drug in 1% or more of PREVACID-treated patients and occurred at a greater rate in PREVACID-treated patients than placebo-treated patients in Table 19.

Table 19: Incidence of Possibly or Probably Treatment-Related Adverse Events in Short-Term, Placebo-Controlled PREVACID Studies

Body System/Adverse Event	PREVACID (N= 2768) %	Placebo (N= 1023) %
Body as a Whole		
Abdominal Pain	2.1	1.2
Digestive System		
Constipation	1.0	0.4
Diarrhea	3.8	2.3
Nausea	1.3	1.2

Headache was also seen at greater than 1% incidence but was more common on placebo. The incidence of diarrhea was similar between patients who received placebo and patients who received 15 mg and 30 mg of PREVACID, but higher in the patients who received 60 mg of PREVACID (2.9%, 1.4%, 4.2%, and 7.4%, respectively).

The most commonly reported possibly or probably treatment-related adverse event during maintenance therapy was diarrhea.

In the risk reduction study of PREVACID for NSAID-associated gastric ulcers, the incidence of diarrhea for patients treated with PREVACID, misoprostol, and placebo was 5%, 22%, and 3%, respectively.

Additional adverse experiences occurring in less than 1% of patients or subjects who received PREVACID in domestic trials are shown below:

Body as a Whole – abdomen enlarged, allergic reaction, asthenia, back pain, candidiasis, carcinoma, chest pain (not otherwise specified), chills, edema, fever, flu syndrome, halitosis, infection (not otherwise specified), malaise, neck pain, neck rigidity, pain, pelvic pain; *Cardiovascular System* - angina, arrhythmia, bradycardia, cerebrovascular accident/cerebral infarction, hypertension/hypotension, migraine, myocardial infarction, palpitations, shock (circulatory failure), syncope, tachycardia, vasodilation; *Digestive System* – abnormal stools, anorexia, bezoar, cardiospasm, cholelithiasis, colitis, dry mouth, dyspepsia, dysphagia, enteritis, eructation, esophageal stenosis, esophageal ulcer, esophagitis, fecal discoloration, flatulence, gastric nodules/fundic gland polyps, gastritis, gastroenteritis, gastrointestinal anomaly, gastrointestinal disorder, gastrointestinal hemorrhage, glossitis, gum hemorrhage, hematemesis, increased appetite, increased salivation, melena, mouth ulceration, nausea and vomiting, nausea and vomiting and diarrhea, oral moniliasis, rectal disorder, rectal hemorrhage, stomatitis, tenesmus, thirst, tongue disorder, ulcerative colitis, ulcerative stomatitis; *Endocrine System* - diabetes mellitus, goiter, hypothyroidism; *Hemic and Lymphatic System* - anemia, hemolysis, lymphadenopathy; *Metabolic and Nutritional Disorders* - gout, dehydration, hyperglycemia/hypoglycemia, peripheral edema, weight gain/loss; *Musculoskeletal System* - arthralgia, arthritis, bone disorder, joint disorder, leg cramps, musculoskeletal pain, myalgia, myasthenia, synovitis; *Nervous System* – abnormal dreams, agitation, amnesia, anxiety, apathy, confusion, convulsion, depersonalization, depression, diplopia, dizziness, emotional lability, hallucinations, hemiplegia, hostility aggravated, hyperkinesia, hypertonia, hypesthesia, insomnia, libido decreased/increased, nervousness, neurosis, paresthesia, sleep disorder, somnolence, thinking abnormality, tremor, vertigo; *Respiratory System* - asthma, bronchitis, cough increased, dyspnea, epistaxis, hemoptysis, hiccup, laryngeal neoplasia, pharyngitis, pleural disorder, pneumonia, respiratory disorder, upper respiratory inflammation/infection, rhinitis, sinusitis, stridor; *Skin and Appendages* - acne, alopecia, contact dermatitis, dry skin, fixed eruption, hair disorder, maculopapular rash, nail disorder, pruritus, rash, skin carcinoma, skin disorder, sweating, urticaria; *Special Senses* – abnormal vision, blurred vision, conjunctivitis, deafness, dry eyes, ear disorder, eye pain, otitis media, parosmia, photophobia, retinal degeneration, taste loss, taste perversion, tinnitus, visual field defect; *Urogenital System* - abnormal menses, breast enlargement, breast pain, breast tenderness, dysmenorrhea, dysuria, gynecomastia, impotence, kidney calculus, kidney pain, leukorrhea, menorrhagia, menstrual disorder, penis disorder, polyuria, testis disorder, urethral pain, urinary frequency, urinary tract infection, urinary urgency, urination impaired, vaginitis.

Postmarketing

ADDITIONAL ADVERSE EXPERIENCES HAVE BEEN REPORTED SINCE PREVACID HAS BEEN MARKETED. THE MAJORITY OF THESE CASES ARE FOREIGN-SOURCED AND A RELATIONSHIP TO PREVACID HAS NOT BEEN ESTABLISHED. BECAUSE THESE EVENTS WERE REPORTED VOLUNTARILY FROM A POPULATION OF UNKNOWN SIZE, ESTIMATES OF FREQUENCY CANNOT BE MADE. THESE EVENTS ARE LISTED BELOW BY COSTART BODY SYSTEM.

Body as a Whole – anaphylactic/anaphylactoid reactions; *Digestive System* - hepatotoxicity, pancreatitis, vomiting; *Hemic and Lymphatic System* - agranulocytosis, aplastic anemia, hemolytic anemia, leukopenia, neutropenia, pancytopenia, thrombocytopenia, and thrombotic thrombocytopenic purpura; *Musculoskeletal System* - myositis; *Skin and Appendages* – severe dermatologic reactions including erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (some fatal); *Special Senses* - speech disorder; *Urogenital System* – interstitial nephritis, urinary retention.

Combination Therapy with Amoxicillin and Clarithromycin

In clinical trials using combination therapy with PREVACID plus amoxicillin and clarithromycin, and PREVACID plus amoxicillin, no adverse reactions peculiar to these drug combinations were observed. Adverse reactions that have occurred have been limited to those that had been previously reported with PREVACID, amoxicillin, or clarithromycin.

Triple Therapy: PREVACID/amoxicillin/clarithromycin

The most frequently reported adverse events for patients who received triple therapy for 14 days were diarrhea (7%), headache (6%), and taste perversion (5%). There were no statistically significant differences in the frequency of reported adverse events between the 10- and 14-day triple therapy regimens. No treatment-emergent adverse events were observed at significantly higher rates with triple therapy than with any dual therapy regimen.

Dual Therapy: PREVACID/amoxicillin

The most frequently reported adverse events for patients who received PREVACID t.i.d. plus amoxicillin t.i.d. dual therapy were diarrhea (8%) and headache (7%). No treatment-emergent adverse events were observed at significantly higher rates with PREVACID t.i.d. plus amoxicillin t.i.d. dual therapy than with PREVACID alone.

For more information on adverse reactions with amoxicillin or clarithromycin, refer to their package inserts, **ADVERSE REACTIONS** sections.

Laboratory Values

The following changes in laboratory parameters in patients who received PREVACID were reported as adverse events:

Abnormal liver function tests, increased SGOT (AST), increased SGPT (ALT), increased creatinine, increased alkaline phosphatase, increased globulins, increased GGTP, increased/decreased/abnormal WBC, abnormal AG ratio, abnormal RBC, bilirubinemia, eosinophilia, hyperlipemia, increased/decreased electrolytes, increased/decreased cholesterol, increased glucocorticoids, increased LDH, increased/decreased/abnormal platelets, and increased gastrin levels. Urine abnormalities such as albuminuria, glycosuria, and hematuria were also reported. Additional isolated laboratory abnormalities were reported.

In the placebo controlled studies, when SGOT (AST) and SGPT (ALT) were evaluated, 0.4% (4/978) and 0.4% (11/2677) patients, who received placebo and PREVACID, respectively, had enzyme elevations greater than three times the upper limit of normal range at the final treatment visit. None of these patients who received PREVACID reported jaundice at any time during the study.

In clinical trials using combination therapy with PREVACID plus amoxicillin and clarithromycin, and PREVACID plus amoxicillin, no increased laboratory abnormalities particular to these drug combinations were observed.

For more information on laboratory value changes with amoxicillin or clarithromycin, refer to their package inserts, **ADVERSE REACTIONS** section.

OVERDOSAGE

PREVACID is not removed from the circulation by hemodialysis. In one reported overdose, a patient consumed 600 mg of PREVACID with no adverse reaction.

Oral PREVACID doses up to 5000 mg/kg in rats (approximately 1300 times the 30 mg human dose based on BSA) and in mice (about 675.7 times the 30 mg human dose based on BSA) did not produce deaths or any clinical signs.

DOSAGE AND ADMINISTRATION

PREVACID is available as a capsule, orally disintegrating tablet and oral suspension, and is available in 15 mg and 30 mg strengths. Directions for use specific to the route and available methods of administration for each of these dosage forms is presented below. PREVACID should be taken before eating. PREVACID products SHOULD NOT BE CRUSHED OR CHEWED. In the clinical trials, antacids were used concomitantly with PREVACID.

Renal insufficiency patients and geriatric patients do not require dosage adjustment. However, dose adjustment should be considered in patients with severe liver disease.

Indication	Recommended Dose	Frequency	For Additional Information, See
Duodenal Ulcers			
Short-Term Treatment	15 mg	Once daily for 4 weeks	**INDICATIONS AND USAGE**
Maintenance of Healed	15 mg	Once daily	**CLINICAL STUDIES**
***H. pylori* Eradication to Reduce the Risk of Duodenal Ulcer Recurrence**[†]			
Triple Therapy:			**INDICATIONS AND USAGE**
PREVACID	30 mg	Twice daily (q12h) for 10 or 14 days	
Amoxicillin	1 gram	Twice daily (q12h) for 10 or 14 days	
Clarithromycin	500 mg	Twice daily (q12h) for 10 or 14 days	
Dual Therapy:			**INDICATIONS AND USAGE**
PREVACID	30 mg	Three times daily (q8h) for 14 days	
Amoxicillin	1 gram	Three times daily (q8h) for 14 days	
Benign Gastric Ulcer			**CLINICAL STUDIES**
Short-Term Treatment	30 mg	Once daily for up to 8 weeks	
NSAID-associated Gastric Ulcer			**CLINICAL STUDIES**
Healing	30 mg	Once daily for 8 weeks*	
Risk Reduction	15 mg	Once daily for up to 12 weeks*	
Gastroesophageal Reflux Disease (GERD)			
Short-Term Treatment of Symptomatic GERD	15 mg	Once daily for up to 8 weeks	**CLINICAL STUDIES**
Short -Term Treatment of Erosive Esophagitis	30 mg	Once daily for up to 8 weeks**	**INDICATIONS AND USAGE**
Pediatric (1 to 11 years of age) Short-Term Treatment of Symptomatic GERD and Short-Term Treatment of Erosive Esophagitis			**PEDIATRIC USE**
≤ 30 kg	15 mg	Once daily for up to 12 weeks[+]	
> 30 kg	30 mg	Once daily for up to 12 weeks[+]	
(12 to 17 years of age) Short-Term Treatment of Symptomatic GERD			
Nonerosive GERD	15 mg	Once daily for up to 8 weeks	
Erosive Esophagitis	30 mg	Once daily for up to 8 weeks	
Maintenance of Healing of Erosive Esophagitis	15 mg	Once daily	**CLINICAL STUDIES**
Pathological Hypersecretory Conditions Including Zollinger-Ellison Syndrome	60 mg	Once daily***	**CLINICAL STUDIES**

† Please refer to amoxicillin and clarithromycin full prescribing information for **CONTRAINDICATIONS** and **WARNINGS**, and for information regarding dosing in elderly and renally-impaired patients.

* Controlled studies did not extend beyond indicated duration.

** For patients who do not heal with PREVACID for 8 weeks (5–10%), it may be helpful to give an additional 8 weeks of treatment. If there is a recurrence of erosive esophagitis, an additional 8 week course of PREVACID may be considered.

*** Varies with individual patient. Recommended adult starting dose is 60 mg once daily. Doses should be adjusted to individual patient needs and should continue for as long as clinically indicated. Dosages up to 90 mg b.i.d. have been administered. Daily dose of greater than 120 mg should be administered in divided doses. Some patients with Zollinger-Ellison Syndrome have been treated continuously with PREVACID for more than 4 years.

+ The PREVACID dose was increased (up to 30 mg b.i.d.) in some pediatric patients after 2 or more weeks of treatment if they remained symptomatic. For pediatric patients unable to swallow an intact capsule please see **Administration Options**.

Administration Options

1. PREVACID Delayed-Release Capsules

PREVACID Capsules-Oral Administration

PREVACID Delayed-Release Capsules should be swallowed whole.

Alternatively, for patients who have difficulty swallowing capsules, PREVACID Delayed-Release Capsules can be opened and administered as follows:

- Open capsule.
- Sprinkle intact granules on one tablespoon of either applesauce, ENSURE® pudding, cottage cheese, yogurt or strained pears.
- Swallow immediately.

PREVACID Delayed-Release Capsules may also be emptied into a small volume of either apple juice, orange juice or tomato juice and administered as follows:

- Open capsule.
- Sprinkle intact granules into a small volume of either apple juice, orange juice or tomato juice (60 mL – approximately 2 ounces).
- Mix briefly.
- Swallow immediately.
- To ensure complete delivery of the dose, the glass should be rinsed with two or more volumes of juice and the contents swallowed immediately.

USE IN OTHER FOODS AND LIQUIDS HAS NOT BEEN STUDIED CLINICALLY AND IS THEREFORE NOT RECOMMENDED.

PREVACID Capsules - Nasogastric Tube Administration

For patients who have a nasogastric tube in place, PREVACID Delayed-Release Capsules can be administered as follows:

- Open capsule.
- Mix intact granules into 40 mL of apple juice. DO NOT USE OTHER LIQUIDS.
- Inject through the nasogastric tube into the stomach.
- Flush with additional apple juice to clear the tube.

2. PREVACID SoluTab Delayed-Release Orally Disintegrating Tablets

PREVACID SoluTab should not be chewed. Place the tablet on the tongue and allow it to disintegrate, with or without water, until the particles can be swallowed. The tablet typically disintegrates in less than 1 minute.

Alternatively, for children or other patients who have difficulty swallowing tablets, PREVACID SoluTab can be delivered in two different ways.

PREVACID SoluTab – Oral Syringe

For administration via oral syringe, PREVACID SoluTab can be administered as follows:

- Place a 15 mg tablet in oral syringe and draw up approximately 4 mL of water, or place a 30 mg tablet in oral syringe and draw up approximately 10 mL of water.
- Shake gently to allow for a quick dispersal.
- After the tablet has dispersed, administer the contents within 15 minutes.
- Refill the syringe with approximately 2 mL (5 mL for the 30 mg tablet) of water, shake gently, and administer any remaining contents.

PREVACID SoluTab – Nasogastric Tube Administration (≥ 8 French)

For administration via a nasogastric tube, PREVACID SoluTab can be administered as follows:

- Place a 15 mg tablet in a syringe and draw up 4 mL of water, or place a 30 mg tablet in a syringe and draw up 10 mL of water.
- Shake gently to allow for a quick dispersal.
- After the tablet has dispersed, inject through the nasogastric tube into the stomach within 15 minutes.
- Refill the syringe with approximately 5 mL of water, shake gently, and flush the nasogastric tube.

3. PREVACID for Delayed-Release Oral Suspension

PREVACID for Delayed-Release Oral Suspension should be administered as follows:

- Open packet.
- To prepare a dose, empty the packet contents into a container containing 2 tablespoons of **WATER**. DO NOT USE OTHER LIQUIDS OR FOODS.
- Stir well, and drink immediately.
- If any material remains after drinking, add more water, stir, and drink immediately.
- **This product should not be given through enteral administration tubes.**

HOW SUPPLIED

PREVACID Delayed-Release Capsules, 15 mg, are opaque, hard gelatin, colored pink and green with the TAP logo and "PREVACID 15" imprinted on the capsules. The 30 mg capsules are opaque, hard gelatin, colored pink and black with the TAP logo and "PREVACID 30" imprinted on the capsules. They are available as follows:

NDC 0300-1541-30 Unit of use bottles of 30: 15-mg capsules
NDC 0300-1541-19 Bottles of 1000: 15-mg capsules
NDC 0300-1541-11 Unit dose package of 100: 15-mg capsules
NDC 0300-3046-13 Bottles of 100: 30-mg capsules
NDC 0300-3046-19 Bottles of 1000: 30-mg capsules
NDC 0300-3046-11 Unit dose package of 100: 30-mg capsules

PREVACID for Delayed-Release Oral Suspension contains white to pale brownish lansoprazole granules and inactive pink granules in a unit dose packet. They are available as follows:
NDC 0300-7309-30 Unit dose carton of 30: 15-mg packets
NDC 0300-7311-30 Unit dose carton of 30: 30-mg packets

PREVACID SoluTab Delayed-Release Orally Disintegrating Tablets, 15 mg, are white to yellowish white uncoated tablets with orange to dark brown speckles, with "15" debossed on one side of the tablet. The 30 mg are white to yellowish white uncoated tablets with orange to dark brown speckles, with "30" debossed on one side of the tablet. The tablets are available as follows:

NDC 0300-1543-30 Unit dose packages of 30: 15-mg tablets
NDC 0300-1544-30 Unit dose packages of 30: 30-mg tablets

Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F). [See USP Controlled Room Temperature]

R_x only

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