

Tablets 20 mg and in 100% of subjects receiving Rabeprazole Sodium Delayed-Release Tablets 40 mg. With Rabeprazole Sodium Delayed-Release Tablets 20 mg and 40 mg per day, significant effects on gastric and esophageal pH were noted after one day of treatment, and more pronounced after seven days of treatment.

Effects on Serum Gastrin
In patients given daily doses of Rabeprazole Sodium Delayed-Release Tablets for up to eight weeks to treat ulcerative or erosive esophagitis and in patients treated for up to 52 weeks to prevent recurrence of disease the median fasting gastrin level increased in a dose-related manner. The group median values stayed within the normal range.

In a group of subjects treated daily with Rabeprazole Sodium Delayed-Release Tablets 20 mg for 4 weeks a doubling of mean serum gastrin concentrations were observed. Approximately 35% of these treated subjects developed serum gastrin concentrations above the upper limit of normal. In a study of CYP2C19 genotyped subjects in Japan, pro-metabolizers developed statistically significantly higher serum gastrin concentrations than extensive metabolizers.

Effects on Enterochromaffin-like (ECL) Cells
Increased serum gastrin secondary to antisecretory agents stimulates proliferation of gastric ECL cells which, over time, may result in ECL cell hyperplasia in rats and mice and gastric carcinoids in rats, especially in females [see *Nonclinical Toxicology* (13.1)].

In over 400 patients treated with Rabeprazole Sodium Delayed-Release Tablets (10 or 20 mg/day) for up to one year, the incidence of ECL cell hyperplasia increased with time and dose, which is consistent with the pharmacological action of the proton pump inhibitor. No patient developed the adenomatoid, dysplastic or neoplastic changes of ECL cells in the gastric mucosa. No patient developed the carcinoid tumors observed in rats.

Endocrine Effects
Studies in humans for up to one year have not revealed clinically significant effects on the endocrine system. In healthy male volunteers treated with Rabeprazole Sodium Delayed-Release Tablets for 13 days, no clinically relevant changes have been detected in the following endocrine parameters examined: 17 β -estradiol, thyroid stimulating hormone, tri-iodothyronine, thyroxine, thyroxine-binding protein, parathyroid hormone, insulin, glucagon, renin, aldosterone, follicle-stimulating hormone, luteinizing hormone, prolactin, somatotrophic hormone, dehydroepiandrosterone, cortisol-binding globulin, and urinary 6 β -hydroxycortisol, serum testosterone and circadian cortisol profile.

Other Effects
In humans treated with Rabeprazole Sodium Delayed-Release Tablets for up to one year, no systemic effects have been observed on the central nervous, lymphoid, hematopoietic, renal, hepatic, cardiovascular, or respiratory systems. No data are available on long-term treatment with Rabeprazole Sodium Delayed-Release Tablets and ocular effects.

Microbiology
The following *in vitro* data are available but the clinical significance is unknown.
Rabeprazole sodium, amoxicillin and clarithromycin as a three drug regimen has been shown to be active against most strains of *Helicobacter pylori* *in vitro* and in clinical infections as described in the *Clinical Studies* (14) and *Indications and Usage* (1) sections.

Helicobacter pylori
Susceptibility testing of *H. pylori* isolates was performed for amoxicillin and clarithromycin using agar dilution methodology^a, and minimum inhibitory concentrations (MICs) were determined.

Standardized susceptibility test procedures require the use of laboratory control microorganisms to control the technical aspects of the laboratory procedures.

Incidence of Antibiotic-Resistant Organisms Among Clinical Isolates
Pretreatment Resistance: Clarithromycin pretreatment resistance rate (MIC ≥ 1 μ g/mL) to *H. pylori* was 9% (51/560) at baseline in all treatment groups combined. A total of 99% (558/560) of patients had *H. pylori* isolates which were considered to be susceptible (MIC ≤ 0.25 μ g/mL) to amoxicillin at baseline. Two patients had baseline *H. pylori* isolates with an amoxicillin MIC of 0.5 μ g/mL.

For susceptibility testing information about Helicobacter pylori, see *Microbiology section in prescribing information for clarithromycin and amoxicillin*.

CLARITHROMYCIN SUSCEPTIBILITY TEST RESULTS AND CLINICAL/BACTERIOLOGIC OUTCOMES^a FOR A THREE DRUG REGIMEN (RABEPRAZOLE 20 MG TWICE DAILY, AMOXICILLIN 1000 MG TWICE DAILY, AND CLARITHROMYCIN 500 MG TWICE DAILY FOR 10 DAYS)

Days of RAC Therapy	Clarithromycin Pretreatment Results	Total Number	H. pylori Negative (Eradicated)	H. pylori Positive (Persistent) Post-Treatment Susceptibility Results			
				S ^b	I ^b	R ^b	No MIC
7	Susceptible ^b	129	103	2	0	1	23
7	Intermediate ^b	0	0	0	0	0	0
7	Resistant ^b	16	5	2	1	4	4
10	Susceptible ^b	133	111	3	1	2	16
10	Intermediate ^b	0	0	0	0	0	0
10	Resistant ^b	9	1	0	0	5	3

^a Includes only patients with pretreatment and post-treatment clarithromycin susceptibility test results.
^b Susceptible (S) MIC ≤ 0.25 μ g/mL, Intermediate (I) MIC = 0.5 μ g/mL, Resistant (R) MIC ≥ 1 μ g/mL.

Patients with persistent *H. pylori* infection following rabeprazole, amoxicillin, and clarithromycin therapy will likely have clarithromycin resistant clinical isolates. Therefore, clarithromycin susceptibility testing should be done when possible. If resistance to clarithromycin is demonstrated or susceptibility testing is not possible, alternative antimicrobial therapy should be instituted.

Amoxicillin Susceptibility Test Results and Clinical/Bacteriological Outcomes: In the U.S. multicenter study, a total of 99% (558/560) of patients had *H. pylori* isolates which were considered to be susceptible (MIC ≤ 0.25 μ g/mL) to amoxicillin at baseline. The other 2 patients had baseline *H. pylori* isolates with an amoxicillin MIC of 0.5 μ g/mL, and both isolates were clarithromycin-resistant at baseline; in one case the *H. pylori* was eradicated. In the 7- and 10-day treatment groups 75% (107/145) and 79% (112/142), respectively, of the patients who had pretreatment amoxicillin susceptible MICs (≤ 0.25 μ g/mL) were eradicated of *H. pylori*. No patients developed amoxicillin-resistant *H. pylori* during therapy.

12.3 Pharmacokinetics
Rabeprazole Sodium Delayed-Release Tablets are enteric-coated to allow rabeprazole sodium, which is acid labile, to pass through the stomach relatively intact.

After oral administration of 20 mg Rabeprazole Sodium Delayed-Release Tablets, peak plasma concentrations (C_{max}) of rabeprazole occur over a range of 2 to 5 hours (T_{max}). The rabeprazole C_{max} and AUC are linear over an oral dose range of 10 mg to 40 mg. There is no appreciable accumulation when doses of 10 mg to 40 mg are administered every 24 hours; the pharmacokinetics of rabeprazole is not altered by multiple dosing.

Absorption: Absolute bioavailability for a 20 mg oral tablet of rabeprazole (compared to intravenous administration) is approximately 52%. When Rabeprazole Sodium Delayed-Release Tablets are administered with a high fat meal, T_{max} is variable, which concomitant food intake may delay the absorption up to 4 hours or longer. However, the C_{max} and the extent of rabeprazole absorption (AUC) are not significantly altered. Thus Rabeprazole Sodium Delayed-Release Tablets may be taken without regard to timing of meals.

Distribution: Rabeprazole is 96.3% bound to human plasma proteins.

Metabolism: Rabeprazole is extensively metabolized. A significant portion of rabeprazole is metabolized via systemic nonenzymatic reduction to a dihydrother compound. Rabeprazole is also metabolized to sulphone and desmethyl compounds via cytochrome P450 in the liver. The biotransfer and sulphone are the primary metabolites measured in human plasma. These metabolites were not observed to have significant antisercretory activity. *In vitro* studies have demonstrated that rabeprazole is metabolized in the liver primarily by cytochromes P450 3A (CYP3A) to a sulphone metabolite and cytochrome P450 2C19 (CYP2C19) to desmethyl rabeprazole. CYP2C19 exhibits a known genetic polymorphism due to its deficiency in some sub-populations (e.g. 3 to 5% of Caucasians and 17 to 20% of Asians). Rabeprazole metabolism is slow in these sub-populations, therefore, they are referred to as poor metabolizers of the drug.

Elimination: Following a single 20 mg oral dose of ¹⁴C-labeled rabeprazole, approximately 90% of the drug was eliminated in the urine, primarily as its biotransfer carboxylic acid, its glucuronide, and mercapturic acid metabolites. The remainder of the dose was recovered in the feces. Total recovery of radioactivity was 99.8%. No unchanged rabeprazole was recovered in the urine or feces.

Geriatric: In 20 healthy elderly subjects administered 20 mg rabeprazole tablet once daily for seven days, AUC values approximately doubled and the C_{max} increased by 60% compared to values in a parallel younger control group. There was no evidence of drug accumulation after once daily administration [see *Use in Special Populations* (8.5)].

Pediatric: The pharmacokinetics of rabeprazole was studied in pediatric patients with GERD aged 12 to 16 years.

Patients 12 to 16 Years of Age
The pharmacokinetics of rabeprazole was studied in 12 adolescent patients with GERD 12 to 16 years of age, in a multicenter study. Patients received rabeprazole 20 mg tablets once daily for five or seven days. An approximate 40% increase in exposure was noted following 5 to 7 days of dosing compared with the exposure after 1 day dosing. Pharmacokinetic parameters in adolescent patients with GERD 12 to 16 years of age were within the range observed in healthy adult volunteers.

Gender and Race: In analyses adjusted for body mass and height, rabeprazole pharmacokinetics showed no clinically significant differences between male and female subjects. In studies that used different formulations of rabeprazole, AUC₀₋₂₄ values for healthy Japanese men were approximately 50-60% greater than values derived from pooled data from healthy men in the United States.

Renal Disease: In 10 patients with stable end-stage renal disease requiring maintenance hemodialysis (creatinine clearance ≤ 5 mL/min/1.73 m²), no clinically significant differences were observed in the pharmacokinetics of rabeprazole after a single 20 mg oral dose when compared to 10 healthy volunteers [see *Dosage and Administration* (2.9)].

Hepatic Disease: In a single dose study of 10 patients with chronic mild to moderate compensated cirrhosis of the liver who were administered a 20 mg dose of rabeprazole, AUC₀₋₂₄ was approximately doubled, the elimination half-life was 2- to 3-fold higher, and total body clearance was decreased to less than half compared to values in healthy men.

In a multiple dose study of 12 patients with mild to moderate hepatic impairment administered 20 mg rabeprazole once daily for eight days, AUC₀₋₂₄ and C_{max} values increased approximately 20% compared to values in healthy age- and gender-matched subjects. These increases were not statistically significant.

No information exists on rabeprazole disposition in patients with severe hepatic impairment. Please refer to the *Dosage and Administration* (2.9) for information on dosage adjustment in patients with hepatic impairment.

Combined Administration with Antimicrobials: Sixteen healthy volunteers genotyped as extensive metabolizers with respect to CYP2C19 were given 20 mg rabeprazole sodium, 1000 mg amoxicillin, 500 mg clarithromycin, or all 3 drugs in a four-way crossover study. Each of the four regimens was administered twice daily for 6 days. The AUC and C_{max} for clarithromycin and amoxicillin were not different following combined administration compared to values for single administration. However, the rabeprazole AUC and C_{max} increased by 11% and 34%, respectively, following combined administration. The AUC and C_{max} for 14-hydroxyclarithromycin (active metabolite of clarithromycin) also increased by 42% and 60%, respectively. This increase in exposure to rabeprazole and 14-hydroxyclarithromycin is not expected to produce safety concerns.

Concomitant Use with Clopidogrel: Clopidogrel is metabolized to its active metabolite in part by CYP2C19. A study of healthy subjects including CYP2C19 extensive and intermediate metabolizers receiving once daily administration of clopidogrel/75 mg concomitantly with placebo or with Rabeprazole Sodium Delayed-Release Tablets 20 mg (n=36), for 7 days was conducted. The mean AUC of the active metabolite of clopidogrel was reduced by approximately 12% (mean AUC ratio was 88%, with 90% CI of 81.7 to 95.5%) when Rabeprazole Sodium Delayed-Release Tablets was coadministered compared to administration of clopidogrel with placebo.

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
In a 88/104-week carcinogenicity study in CD-1 mice, rabeprazole at oral doses up to 100 mg/kg/day did not produce any increased tumor occurrence. The highest tested dose produced a systemic exposure to rabeprazole (AUC) of 1.40 μ g \cdot hr/mL which is 1.6 times the human exposure (plasma AUC₀₋₂₄ = 0.88 μ g \cdot hr/mL) at the recommended dose for GERD (20 mg/day). In a 28-week carcinogenicity study in p53^{-/-} transgenic mice, rabeprazole at oral doses of 20, 60, and 200 mg/kg/day did not cause an increase in the incidence rates of tumors but produced gastric mucosal hyperplasia at all doses. The systemic exposure to rabeprazole at 200 mg/kg/day is about 17-24 times the human exposure at the recommended dose for GERD. In a 104-week carcinogenicity study in Sprague-Dawley rats, males were treated with oral doses of 5, 15, 30 and 60 mg/kg/day and females with 5, 15, 30, 60 and 120 mg/kg/day. Rabeprazole produced gastric enterochromaffin-like (ECL) cell hyperplasia in male and female rats and ECL cell carcinoid tumors in female

rats at all doses including the lowest tested dose. The lowest dose (5 mg/kg/day) produced a systemic exposure to rabeprazole (AUC) of about 0.1 μ g \cdot hr/mL which is about 0.1 times the human exposure at the recommended dose for GERD. In male rats, no treatment related tumors were observed at doses up to 60 mg/kg/day producing a rabeprazole plasma exposure (AUC) of about 0.2 μ g \cdot hr/mL (0.2 times the human exposure at the recommended dose for GERD).

Rabeprazole was positive in the Ames test, the Chinese hamster ovary cell (CHO/HGPR1) forward gene mutation test and the mouse lymphoma cell (L5178Y/TK⁺) forward gene mutation test. Its demethylated-metabolite was also positive in the Ames test. Rabeprazole was negative in the *in vitro* Chinese hamster lung cell chromosome aberration test, the *in vivo* mouse micronucleus test, and the *in vivo* and *ex vivo* rat hepatocyte unscheduled DNA synthesis (UDS) tests.

Rabeprazole at intravenous doses up to 30 mg/kg/day (plasma AUC of 8.8 μ g \cdot hr/mL, about 10 times the human exposure at the recommended dose for GERD) was found to have no effect on fertility and reproductive performance of male and female rats.

13.2 Animal Toxicology and/or Pharmacology
Studies in juvenile and young adult rats and dogs were performed. In juvenile animal studies rabeprazole sodium was administered orally to rats for up to 5 weeks and to dogs for up to 13 weeks, each commencing on Day 7 postpartum and followed by a 13-week recovery period. Rats were dosed at 5, 25 or 150 mg/kg/day and dogs were dosed at 3, 10 or 30 mg/kg/day. The data from these studies were comparable to those reported for young adult animals. Pharmacologically mediated changes, including increased serum gastrin levels and stomach changes, were observed at all dose levels in both rats and dogs. These observations were reversible over the 13-week recovery periods. Although body weights and/or crown-rump lengths were minimally decreased during dosing, no effects on the development parameters were noted in either juvenile rats or dogs.

14 CLINICAL STUDIES
14.1 Healing of Erosive or Ulcerative GERD in Adults
In a U.S. multicenter, randomized, double-blind, placebo-controlled study, 103 patients were treated for up to eight weeks with placebo, 10 mg, 20 mg or 40 mg Rabeprazole Sodium Delayed-Release Tablets OD. For this and all studies of GERD healing, only patients with GERD symptoms and at least grade 2 esophagitis (modified Hetzel-Dent grading scale) were eligible for entry. Endoscopic healing was defined as grade 0 or 1. Each rabeprazole dose was significantly superior to placebo in producing endoscopic healing after four and eight weeks of treatment. The percentage of patients demonstrating endoscopic healing was as follows:

TABLE 7
HEALING OF EROSIIVE OR ULCERATIVE GASTROESOPHAGEAL REFLUX DISEASE (GERD) PERCENTAGE OF PATIENTS HEALED

Week	10 mg Rabeprazole Sodium Delayed-Release Tablets OD N=27	20 mg Rabeprazole Sodium Delayed-Release Tablets OD N=25	40 mg Rabeprazole Sodium Delayed-Release Tablets OD N=26	Placebo N=25
4	63%*	56%*	54%*	0%
8	93%*	84%*	85%*	12%

* (p<0.001 versus placebo)

In addition, there was a statistically significant difference in favor of the Rabeprazole Sodium Delayed-Release Tablets 10 mg, 20 mg, and 40 mg doses compared to placebo at Weeks 4 and 8 regarding complete resolution of GERD heartburn frequency (p<0.026). All Rabeprazole Sodium Delayed-Release Tablets groups reported significantly greater rates of complete resolution of GERD daytime heartburn severity compared to placebo at Weeks 4 and 8 (p<0.036). Mean reductions from baseline in daily antacid dose were statistically significant for all Rabeprazole Sodium Delayed-Release Tablets groups when compared to placebo at both Weeks 4 and 8 (p<0.007).

In a North American multicenter, randomized, double-blind, active-controlled study of 336 patients, Rabeprazole Sodium Delayed-Release Tablets was statistically superior to ranitidine with respect to the percentage of patients healed at endoscopy after four and eight weeks of treatment (see table below):

TABLE 8
HEALING OF EROSIIVE OR ULCERATIVE GASTROESOPHAGEAL REFLUX DISEASE (GERD) PERCENTAGE OF PATIENTS HEALED

Week	Rabeprazole Sodium Delayed-Release Tablets 20 mg OD N=167	Ranitidine 150 mg QID N=169
4	59%*	36%
8	87%*	66%

* (p<0.001 versus ranitidine)

Rabeprazole Sodium Delayed-Release Tablets 20 mg once daily was significantly more effective than ranitidine 150 mg QID in the percentage of patients with complete resolution of heartburn at Weeks 4 and 8 (p<0.001). Rabeprazole Sodium Delayed-Release Tablets 20 mg once daily was also more effective in complete resolution of daytime heartburn (p<0.025), and nighttime heartburn (p<0.012) at both Weeks 4 and 8, with significant differences by the end of the first week of the study.

14.2 Long-term Maintenance of Healing of Erosive or Ulcerative GERD in Adults
The long-term maintenance of healing in patients with erosive or ulcerative GERD previously healed with gastric antisecretory therapy was assessed in two U.S. multicenter, randomized, double-blind, placebo-controlled studies of identical design of 52 weeks duration. The two studies randomized 209 and 285 patients, respectively, to receive either 10 mg or 20 mg of Rabeprazole Sodium Delayed-Release Tablets OD or placebo. As demonstrated in the tables below, Rabeprazole Sodium Delayed-Release Tablets was significantly superior to placebo in both studies with respect to the maintenance of healing of GERD and the proportions of patients remaining free of heartburn symptoms at 52 weeks:

TABLE 9
PERCENT OF PATIENTS IN ENDOSCOPIC REMISSION

	Rabeprazole Sodium Delayed-Release Tablets 10 mg	Rabeprazole Sodium Delayed-Release Tablets 20 mg	Placebo
Study 1	N=66	N=67	N=70
Week 4	83%*	96%*	44%
Week 13	79%*	93%*	39%
Week 26	77%*	93%*	31%
Week 39	76%*	91%*	30%
Week 52	73%*	90%*	29%
Study 2	N=83	N=83	N=89
Week 4	89%*	94%*	40%
Week 13	86%*	91%*	33%
Week 26	85%*	89%*	30%
Week 39	84%*	88%*	29%
Week 52	77%*	86%*	29%

COMBINED STUDIES N=159 N=160 N=169

Week 4	87%*	94%*	42%
Week 13	83%*	92%*	36%
Week 26	82%*	91%*	31%
Week 39	81%*	89%*	30%
Week 52	75%*	87%*	29%

* (p<0.001 versus placebo)

TABLE 10
PERCENT OF PATIENTS WITHOUT RELAPSE IN HEARTBURN FREQUENCY AND DAYTIME AND NIGHTTIME HEARTBURN SEVERITY AT WEEK 52

	Rabeprazole Sodium Delayed-Release Tablets 10 mg	Rabeprazole Sodium Delayed-Release Tablets 20 mg	Placebo
Heartburn Frequency			
Study 1	46/55 (84%)*	48/52 (92%)*	17/45 (38%)
Study 2	50/72 (69%)*	57/72 (79%)*	22/79 (28%)
Daytime Heartburn Severity			
Study 1	61/64 (95%)*	60/62 (97%)*	42/61 (69%)
Study 2	73/84 (87%)*†	82/87 (94%)*	67/90 (74%)
Nighttime Heartburn Severity			
Study 1	57/61 (93%)*	60/61 (98%)*	37/56 (66%)
Study 2	67/80 (84%)*	79/87 (91%)*†	64/87 (74%)

* p<0.001 versus placebo
† 0.001-p<0.05 versus placebo

14.3 Treatment of Symptomatic GERD in Adults
Two U.S. multicenter, double-blind, placebo controlled studies were conducted in 316 adult patients with daytime and nighttime heartburn. Patients reported 5 or more periods of moderate to very severe heartburn during the placebo treatment phase the week prior to randomization. Patients were confirmed by endoscopy to have no esophageal erosions.

The percentage of heartburn free daytime and/or nighttime periods was greater with Rabeprazole Sodium Delayed-Release Tablets 20 mg compared to placebo over the 4 weeks of study in Study RAB-USA-2 (47% vs 23%) and Study RAB-USA-3 (52% vs 28%). The mean decreases from baseline in average daytime and nighttime heartburn scores were significantly greater for Rabeprazole Sodium Delayed-Release Tablets 20 mg as compared to placebo at week 4. Graphical displays depicting the daily mean daytime and nighttime scores are provided in Figures 2 to 5.

FIGURE 2: MEAN DAYTIME HEARTBURN SCORES RAB-USA-2

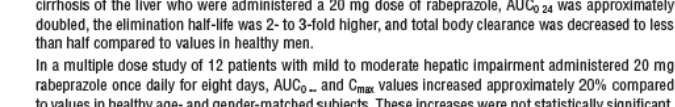


FIGURE 3: MEAN NIGHTTIME HEARTBURN SCORES RAB-USA-2

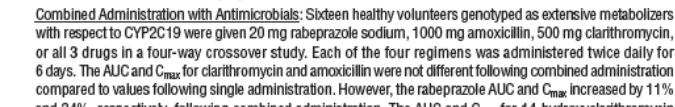


FIGURE 4: MEAN DAYTIME HEARTBURN SCORES RAB-USA-3

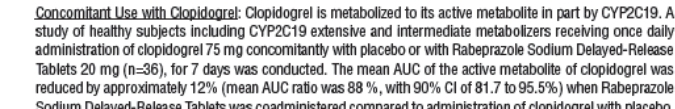
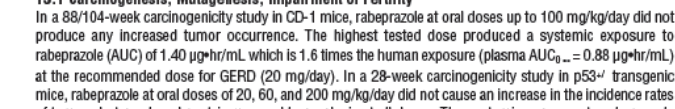


FIGURE 5: MEAN NIGHTTIME HEARTBURN SCORES RAB-USA-3



In addition, the combined analysis of these two studies showed Rabeprazole Sodium Delayed-Release Tablets 20 mg significantly improved other GERD-associated symptoms (regurgitation, belching and early satiety) by week 4 compared with placebo (all p values < 0.005).

Rabeprazole Sodium Delayed-Release Tablets 20 mg also significantly reduced daily antacid consumption versus placebo over 4 weeks (p<0.001).

14.4 Healing of Duodenal Ulcers in Adults
In a U.S., randomized, double-blind, multicenter study assessing the effectiveness of 20 mg and 40 mg of Rabeprazole Sodium Delayed-Release Tablets OD versus placebo for healing endoscopically defined duodenal ulcers, 100 patients were treated for up to four weeks. Rabeprazole Sodium Delayed-Release Tablets was significantly superior to placebo in producing healing of duodenal ulcers. The percentages of patients with endoscopic healing are presented below:

TABLE 11
HEALING OF DUODENAL ULCERS PERCENTAGE OF PATIENTS HEALED

Week	Rabeprazole Sodium Delayed-Release Tablets 20 mg OD N=34	Rabeprazole Sodium Delayed-Release Tablets 40 mg OD N=33	Placebo N=33
2	44%	42%	21%
4	79%*	91%*	39%

* (p<0.001 versus placebo)

At Weeks 2 and 4, significantly more patients in the Rabeprazole Sodium Delayed-Release Tablets 20 mg and 40 mg groups reported complete resolution of ulcer pain frequency (p<0.018), daytime pain severity (p<0.023), and nighttime pain severity (p<0.035) compared with placebo patients. The only exception was the Rabeprazole Sodium Delayed-Release Tablets 40 mg group versus placebo at Week 2 for duodenal ulcer pain frequency (p=0.094). Significant differences in resolution of daytime and nighttime pain were noted in both Rabeprazole Sodium Delayed-Release Tablets groups relative to placebo by the end of the first week of the study. Significant reductions in daily antacid use were also noted in both Rabeprazole Sodium Delayed-Release Tablets groups compared to placebo at Weeks 2 and 4 (p<0.001).

An international randomized, double-blind, active-controlled trial was conducted in 205 patients comparing 20 mg Rabeprazole Sodium Delayed-Release Tablets OD with 20 mg omeprazole OD. The study was designed to provide at least 80% power to exclude a difference of at least 10% between Rabeprazole Sodium Delayed-Release Tablets and omeprazole, assuming four-week healing response rates of 93% for both groups. In patients with endoscopically defined duodenal ulcers treated for up to four weeks, Rabeprazole Sodium Delayed-Release Tablets was comparable to omeprazole in producing healing of duodenal ulcers. The percentages of patients with endoscopic healing at two and four weeks are presented below:

TABLE 12
HEALING OF DUODENAL ULCERS PERCENTAGE OF PATIENTS HEALED

Week	Rabeprazole Sodium Delayed-Release Tablets 20 mg OD N=102	Omeprazole 20 mg OD N=103	95% Confidence Interval for the Treatment Difference (Rabeprazole Sodium Delayed-Release Tablets - Omeprazole)
2	69%	61%	(-6%, 22%)
4	98%	93%	(-3%, 15%)

Rabeprazole Sodium Delayed-Release Tablets and omeprazole were comparable in providing complete resolution of symptoms.

14.5 Helicobacter pylori Eradication in Patients with Peptic Ulcer Disease or Symptomatic Non-Ulcer Disease in Adults
The U.S. multicenter study was a double-blind, parallel-group comparison of rabeprazole, amoxicillin, and clarithromycin for 3, 7, or 10 days vs. omeprazole, amoxicillin and clarithromycin for 10 days. Therapy consisted of rabeprazole 20 mg twice daily, amoxicillin 1000 mg twice daily, and clarithromycin 500 mg twice daily (RAC) or omeprazole 20 mg twice daily, amoxicillin 1000 mg twice daily, and clarithromycin 500 mg twice daily (OAC). Patients with *H. pylori* infection were stratified in a 1:1 ratio for those with peptic ulcer disease (active or a history of ulcer in the past five years) [PU] and those who were symptomatic but without peptic ulcer disease [NPU], as determined by upper gastrointestinal endoscopy. The overall *H. pylori* eradication rates, defined as negative ¹⁴C-UBT for *H. pylori* ≥ 6 weeks from the end of the treatment are shown in the following table. The eradication rates in the 7-day and 10-day RAC regimens were found to be similar to 10-day OAC regimen using either the Intent-to-Treat (ITT) or Per-Protocol (PP) populations. Eradication rates in the RAC 3-day regimen were inferior to the other regimens.

TABLE 13
HELICOBACTER PYLORI ERADICATION AT ≥ 6 WEEKS AFTER THE END OF TREATMENT