TRI-POWER IN ACTION

SPEED.EFFICACY.SAFETY

Pariet®, the PPI that provides the fastest rate of acid inhibition in 5 minutes with minimal drug to drug interaction

HI-Eisai

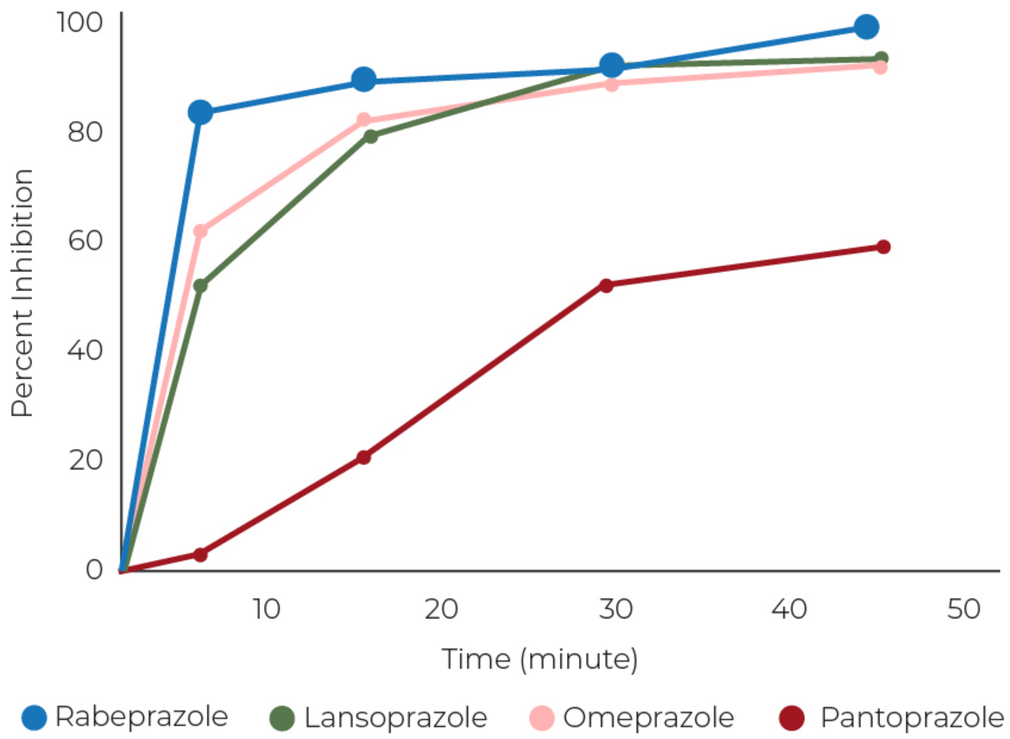
hhc human health care

Rabeprazole sodium

Pariet®

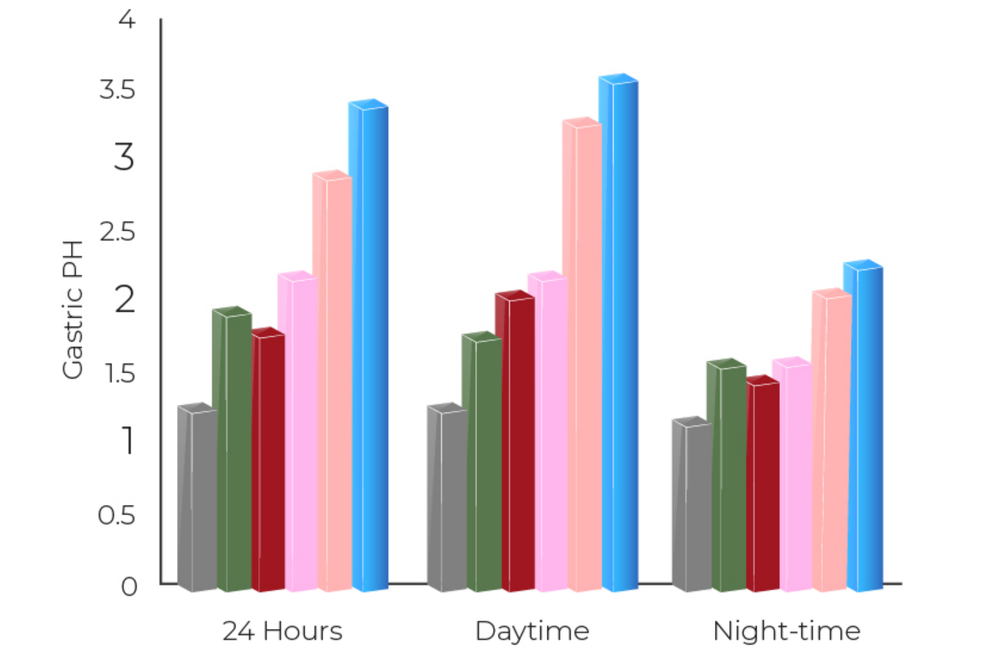
Pariet®, the PPI that provides the fastest rate of acid inhibition in 5 minutes with minimal drug to drug interaction

Fastest acid inhibition versus other PPIs in just 5 minutes



M. Besancon et. al., Jour Bio. Vol 272, 1997

Provides greatest acid control during the first 24 hours of treatment



*P <0.05 vs. all other PPIs and placebo

D. Pantoflickova et. al.. Aliment Pharmacol Ther., 2003

PH-PR-CA-22C-01

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Rabeprazole sodium

Pariet®

Pariet® has the fastest acid inhibition in just 5 minutes

Rabeprazole

100%
Acid inhibition
in 5 Minutes

Pantoprazole

20%
Acid inhibition
in 10 Minutes

Lansoprazole

66%
Acid inhibition
in 10 Minutes

Omeprazole

47%
Acid inhibition
in 10 Minutes

Pariet® provides greatest acid control during the first 24 hours of treatment

24 Hours
Gastric pH

Rabeprazole **3.4**

Lansoprazole	2.9
Pantoprazole	2.2
Omeprazole 20mg (Caps)	1.9
Omeprazole 20mg (MUPS)	1.8
Placebo	1.3

Daytime
Gastric pH

Rabeprazole **3.6**

Lansoprazole	3.3
Pantoprazole	2.2
Omeprazole 20mg (Caps)	1.8
Omeprazole 20mg (MUPS)	2.1
Placebo	1.3

Night-time
Gastric pH

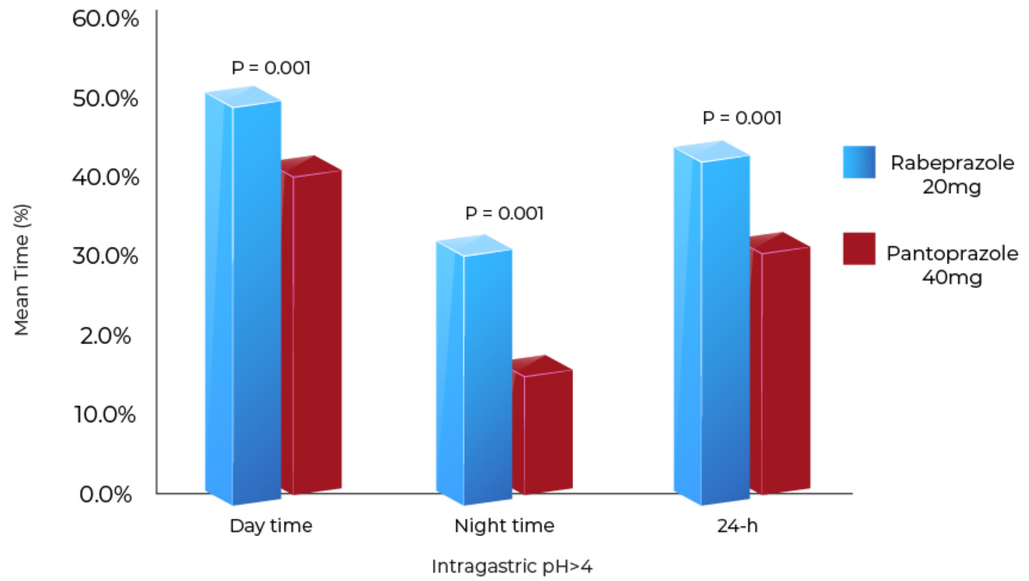
Rabeprazole **2.3**

Lansoprazole	2.1
Pantoprazole	1.6
Omeprazole 20mg (Caps)	1.5
Omeprazole 20mg (MUPS)	1.2
Placebo	1.2

p <0.05 vs. all other PPIs and placebo

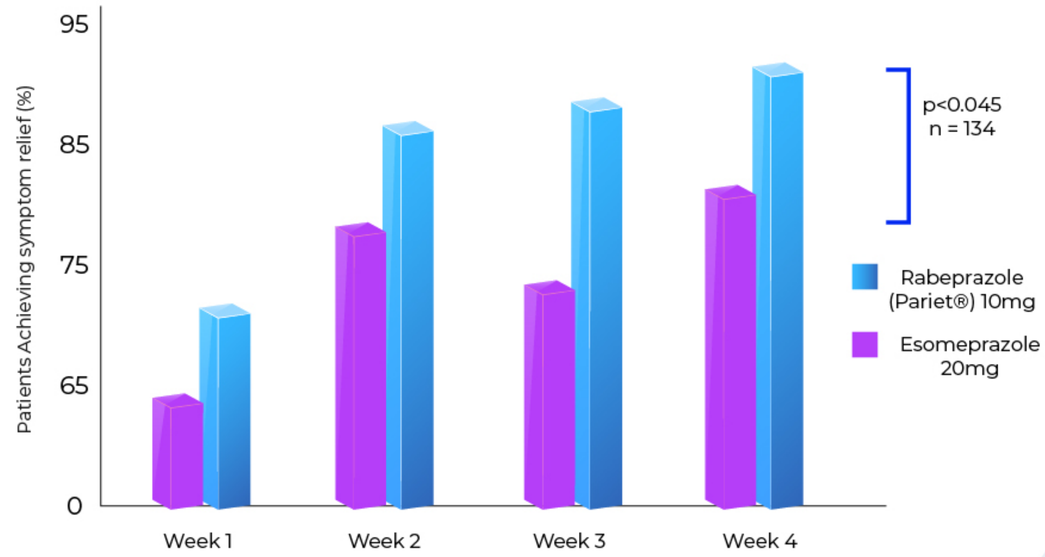
Pariet®, the PPI that provides the fastest rate of acid inhibition in 5 minutes with minimal drug interaction

Rabeprazole is significantly more effective in mean percentage of time with intragastric pH>4 during daytime, night-time and 24-h period than pantoprazole



Miner et. Al. Aliment Pharmacol Ther. 31,991-1000

Rabeprazole provides satisfactory relief of day-time heartburn and regurgitation compared to esomeprazole



Fock KM, et al. World J Gastroenterol 2005; 11(20):3091-B

Rabeprazole sodium

Pariet®

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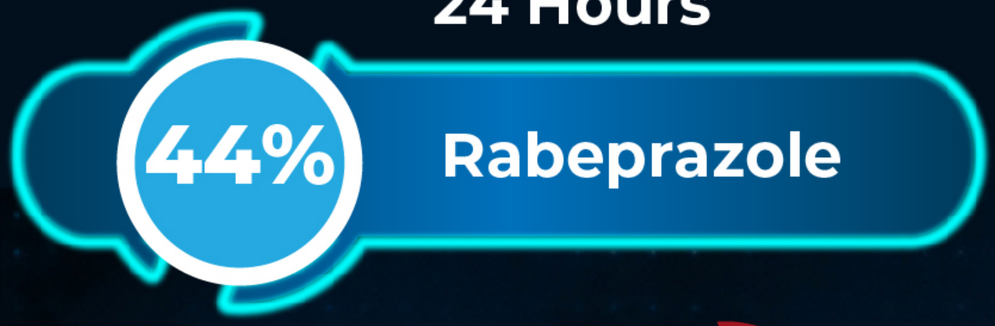
Pariet® is significantly more effective in mean percentage of time with intragastric pH>4 during daytime, night-time and 24-h period than pantoprazole

24 Hours



p value = 0.001

Daytime

p value = 0.001

Night-time

p value = 0.001

Pariet® provides satisfactory relief of day-time heartburn and regurgitation compared to esomeprazole

Week 1

Rabeprazole **71.1%**

Esomeprazole **60.5%**

p value = 0.045
N = 134

Week 2

Rabeprazole **85.7%**

Esomeprazole **75.7%**

p value = 0.045
N = 134

Week 3

Rabeprazole **86%**

Esomeprazole **71.4%**

p value = 0.045
N = 134

Week 4

Rabeprazole **92.5%**

Esomeprazole **79.4%**

p value = 0.045
N = 134

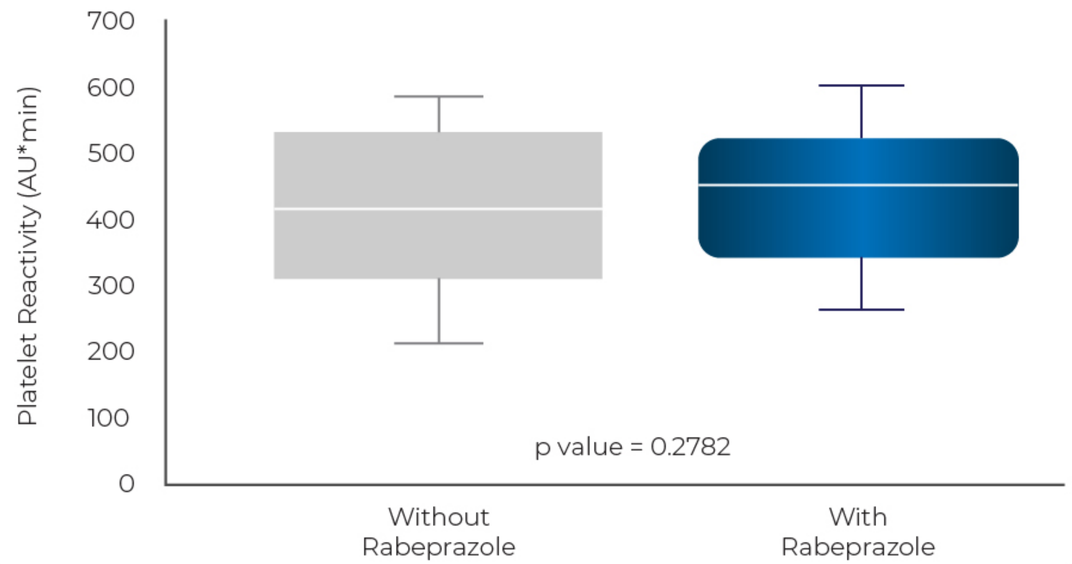
Pariet®, the PPI that provides the fastest rate of acid inhibition in 5 minutes with minimal drug to drug interaction

Has minimal drug interaction when compared to other PPI's

PPI	Diazepam	Warfarin	Phenytoin	Theophylline
Rabeprazole	-	-	-	-
Omeprazole	+	+	+	-*
Esomeprazole	+	+	+	?*
Lansoprazole	-	+	-	-*
Pantoprazole	-	-	-	-

Humphries et al. Gastroenterology 1996; 110 (suppl): A138 , Humphries et al. Gut 1996; 39 (suppl 3): A47
Ishizaki et al. Clin Pharmacol Ther 1995; 58: 155-164, Andersson. Clin Pharmacokinet 1996; 31 :9-28

Does not significantly affect the clopidogrel induced platelet inhibition



Hokimoto S, et al. Circulation 2014; 120: S1033.

ESC 2017 GUIDELINES

While the evidence that a PPI does not increase the risk of cardiovascular events was generated with omeprazole, based on a drug-drug interaction studies, omeprazole and esomeprazole would appear to have the highest propensity for clinically relevant interactions, while pantoprazole and Rabeprazole have the lowest.

Rabeprazole sodium

Pariet®

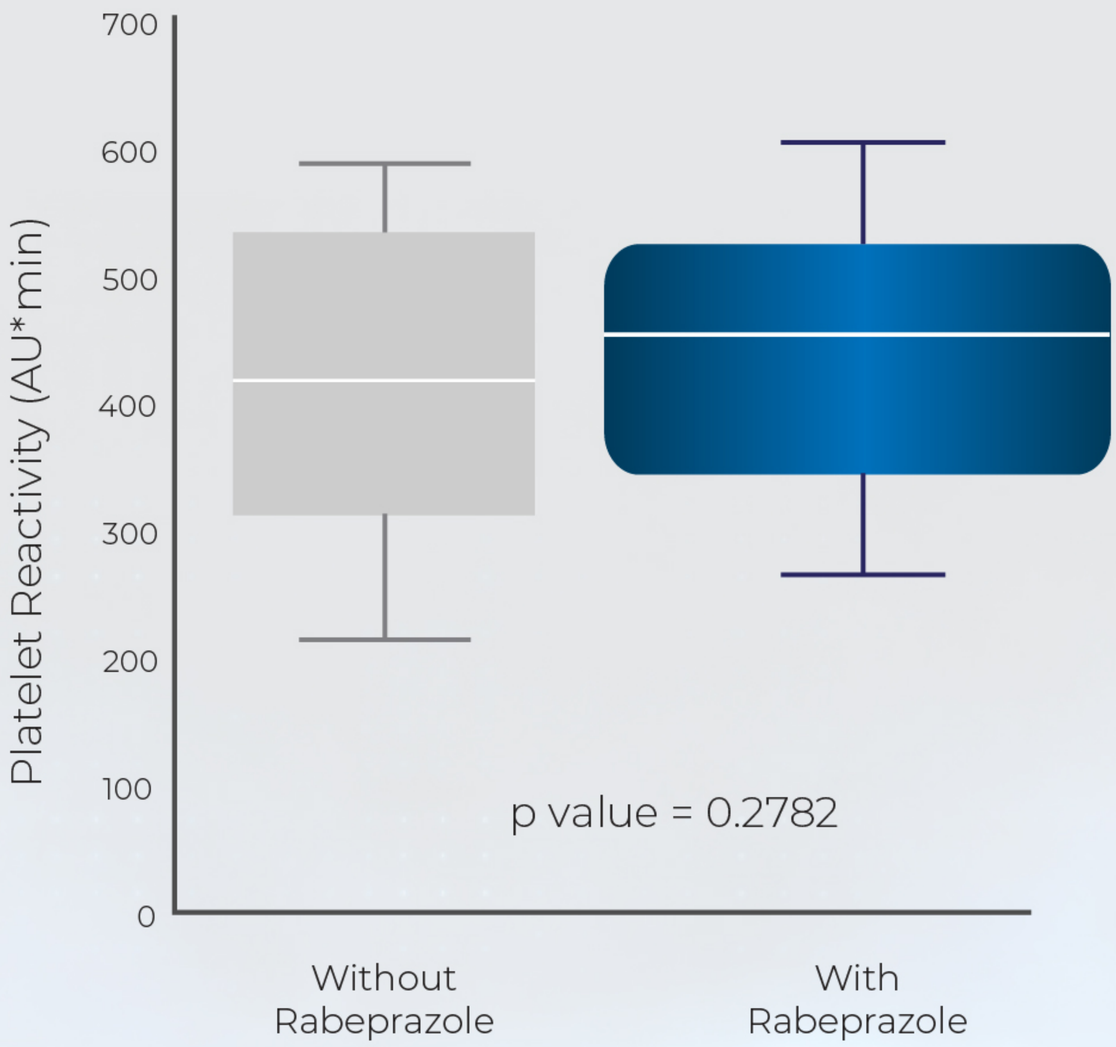
SPEED.EFFICACY.SAFETY

PH-PR-CA-22C-01

Has minimal drug interaction when compared to other PPI's

PPI	Diazepam	Warfarin	Phenytoin	Theophylline
Rabeprazole	-	-	-	-
Omeprazole	+	+	+	-*
Esomeprazole	+	+	+	?*
Lansoprazole	-	+	-	-*
Pantoprazole	-	-	-	-

Does not significantly affect the clopidogrel induced platelet inhibition



ESC 2017 GUIDELINES

- Omeprazole & Esomeprazole - Highest propensity for clinically relevant interactions
- **Rabeprazole** & Pantoprazole – lowest propensity for clinically relevant interactions

Pariet®, the innovator Rabeprazole now made more affordable at almost 50% discount in all Mercury Drugstore and Med Express branches

Rabeprazole sodium
Pariet®

HI-Eisai
human health care

PasyenTipid

Get a special discount from the participating products:

20 mg
Less Php 50.50

Save 48%
When you buy 1 tablet

1. Purchase of this medicine requires a doctor's prescription.
2. This coupon is only redeemable at any Mercury Drug store

Med EXPRESS Drugstore
The No. 1 Hospital Outpatient Pharmacy

PATIENT COMPLIANCE PROGRAM

1. Present the doctor's prescription.
2. Purchase a minimum of 7 tablets of Pariet 20mg to get **50% discount**

SPEED.EFFICACY.SAFETY

Daily Treatment Cost

Brand Name	Generic Name	Recommended Dose	SKU	Daily Treatment Cost (Cost/Tab)	With Pasyentipid and Medexpress Discount	Cost Saving
Pariet	**Rabeprazole**	**OD**	**10 mg**	**79.00**	**54.50**	-
			20 mg	**105.00**		-
Brand Nex	Esomeprazole	OD	20 mg	134..75		80.25
			40 mg	148.75		94.25
Brand Pan	Pantoprazole	OD	20 mg	71.00		16.50
			40 mg	104.00		49.50
Brand Dex	Dexlansoprazole	OD	30 mg	83.00		28.50
			60 mg	106.00		51.50
Brand Pre	Lansoprazole	OD	15 mg	68.00		13.50
			30 mg	104.00		49.50

*Mercury Price Survey as of September 2022
**MIMS Drug Reference 2019

Rabeprazole sodium
Pariet®

PH-PR-CA-22C-01

Pariet®, the innovator Rabeprazole now made more affordable at 50% discount in all Mercury Drugstore and Med Express branches

Rabeprazole sodium

Pariet®

Hi-Eisai hhe human health care

PasyenTipid

Get a special discount from the participating products:

20 mg

Less Php 50.50

Save 50% When you buy 1 tablet

1. Purchase of this medicine requires a doctor's prescription.
2. This coupon is only redeemable at any Mercury Drug store

MedEXPRESS Drugstore

The No. 1 Hospital Outpatient Pharmacy

PATIENT COMPLIANCE PROGRAM

1. Present the doctor's prescription.
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Daily Treatment Cost

Brand Name	Generic Name	Recommended Dose	SKU	Cost/Tab	Daily Treatment Cost	With 50% discount through Pasyentipid and Medexpress	Cost Saving
Pariet	**Rabeprazole**	**OD**	**10 mg**	**76.00**	**76.00**	**76.00**	-
			20 mg	**101.00**	**101.00**	**50.50**	-
Brand Nex	Esomeprazole	OD	20 mg	130.75	130.75		54.75
			40 mg	144.25	144.25		93.75
Brand Pan	Pantoprazole	OD	20 mg	71.00	71.00		- 5.00
			40 mg	104.00	104.00		53.50
Brand Dex	Dexlansoprazole	OD	30 mg	83.00	83.00		7.00
			60 mg	106.00	106.00		55.50
Brand Pre	Lansoprazole	OD	15 mg	68.00	68.00		- 8.00
			30 mg	104.00	104.00		53.50

*Mercury Price Survey as of March 2022
**MIMS Drug Reference 2019

SPEED.EFFICACY.SAFETY

Rabeprazole sodium

Pariet®

PH-PR-CA-22C-01

Product Insert

Rabeprazole sodium

Pariet®

10 mg & 20 mg Tablets

Please consult full prescribing information before prescribing

Formulation: Each gastro-resistant tablet contains 10 mg or 20 mg of rabeprazole sodium.

Indications: For the treatment of active duodenal ulcer, active benign gastric ulcer, anastomotic ulcer , erosive or ulcerative gastro-esophageal reflux disease (GERD), GERD maintenance, symptomatic GERD, eradication of Helicobacter pylori in patients with peptic ulcer diseases, Zollinger-Ellison Syndrome (ZES), prevention of gastric and duodenal ulcer recurrences associated with low-dose pain aspirin therapy and other pathological hypersecretory conditions.

Dosage and Administration: Active duodenal ulcer, active benign gastric ulcer and anastomotic ulcer: 10 mg or 20 mg once a day taken in the a.m.; erosive or ulcerative gastroesophageal reflux disease: 10 mg or 20 mg once a day to be taken for 4 to 8 wks. Doses of 10 mg or 20 mg twice daily may be administered orally for another eight weeks in reflux esophagitis patients who are not responding to the usual dose of proton pump inhibitors. However, a dose of 20 mg twice daily should only be administered to patients with severe mucosa injury;

Gastroesophageal reflux maintenance: 10 mg to 20 mg once a day depending upon patient response; symptomatic gastroesophageal reflux disease: 10 mg once a day in patients without esophagitis. Zollinger-Ellison syndrome and other hypersecretory conditions: 60 mg once or twice daily up to 100 mg once a day: eradication of H. pylori: rabeprazole sodium 10 mg or 20 mg twice daily + clarithromycin 500 mg twice daily with amoxicillin 1 g twice daily; for the prevention of gastric and duodenal ulcer recurrences associated with low-dose aspirin therapy, the usual dosage for adults is 10 mg administered orally once a day or as prescribed.

Contraindications: Hypersensitivity to rabeprazole sodium, substituted benzimidazoles or to any excipient used in the formulation, Pregnancy and breast feeding.

Special Warnings and Precautions for Use: Symptomatic response to therapy with sodium rabeprazole does not preclude the presence of gastric or esophageal malignancy therefore the possibility of malignancy should be excluded prior to commencing treatment with Rabeprazole sodium (PARIET®).

Patients on long-term treatment (particularly those treated for more than a year) should be kept under regular surveillance.

No evidence of significant drug related safety problems was seen in a study of patients with mild to moderate hepatic impairment versus normal age and sex matched controls. However because there are no clinical data on the use of Rabeprazole sodium (PARIET®) in the treatment of patients with severe hepatic dysfunction the prescriber is advised to exercise caution when treatment with Rabeprazole sodium (PARIET®) is first initiated in such patients. The exposure to rabeprazole sodium (AUC) in patients with significant hepatic dysfunction is approximately two-fold that of healthy patients.

Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPIs for at least three months, in most cases after a year of therapy. Serious adverse events include tetany, arrhythmias, and seizures. In most patients, treatment of hypomagnesemia required magnesium replacement and discontinuation of the PPI.

For patients expected to be on prolonged treatment or who take PPIs with medications such as digoxin or drugs that may cause hypomagnesemia (e.g., diuretics), health care professionals may consider monitoring magnesium levels prior to initiation of PPI treatment and periodically.

Fractures

Observational studies suggest that proton pump inhibitor (PPI) therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine. The risk of fracture was increased in patients who received high-dose, and long-term PPI therapy (a year or longer).

Concomitant use of Rabeprazole with Methotrexate

Literature suggests that concomitant use of PPIs with methotrexate (primarily at high dose; see methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or its metabolite, possibly leading to methotrexate toxicities. In high-dose methotrexate administration, a temporary withdrawal of the PPI may be considered in some patients.

Clostridium difficile

Treatment with proton pump inhibitors may possibly increase the risk of gastrointestinal infections such as Clostridium difficile.

Subacute cutaneous lupus erythematosus

Subacute cutaneous lupus erythematosus (SCLE) has been reported with the use of Proton Pump Inhibitors (PPIs). If lesions occur, especially in sun-exposed areas of the skin, and if accompanied by arthralgia, the patient should seek medical help promptly and the health care professional should consider stopping rabeprazole. The occurrence of SCLE with previous PPI treatment may increase the risk of SCLE with other PPIs.

Side Effects: Headache, diarrhea,abdominal pain, asthenia, flatulence, rash and dry mouth. Insomnia, infection, dizziness, cough, pharyngitis, rhinitis, vomiting, nausea, constipation, non-specific pain, back pain, flu-like syndrome.

Drug Interactions: Ketoconazole, itraconazole, atazanavir, ritonavir.

Pharmacodynamics:

Mechanism of Action: Rabeprazole sodium belongs to the class of anti-secretory compounds, the substituted benzimidazoles, that do not exhibit anticholinergic or H2-histamine antagonist properties, but supress gastric acid secretion by the specific inhibition of the H+/K+-ATPase enzyme (the acid or proton pump). The effect is dose-related and leads to inhibition of both basal and stimulated acid secretion irrespective of the stimulus. Animal studies indicate that after administration, rabeprazole sodium rapidly disappears from both the plasma and gastric mucosa. As a weak base, rabeprazole is rapidly absorbed following all doses and is concentrated in the acid environment of the parietal cells. Rabeprazole is converted to the active sulphenamide form through protonation and it subsequently reacts with the available cysteines on the proton pump.

Anti-secretory Activity: After oral administration of a 20 mg dose of rabeprazole sodium the onset of the anti-secretory effect occurs within one hour with the maximum effect occuring within two to four hours. Inhibition of basal and food stimulated acid secretion 23 hours after the first dose of rabeprazole sodium are 69% and 82% respectively and the duration of inhibition lasts up to 48 hours. The inhibitory effect of rabeprazole sodium on acid secretion increases slightly with repeated once-daily dosing achieving steady state inhibition after three days. When the drug is discontinued, secretory activity normalizes over 2 to 3 days.

Serum Gastrin Effects: In clinical studies patients were treated once daily with 10 or 20mg rabeprazole sodium, for up to 43 months duration. Serum gastrin levels increased during the first 2 to 8 weeks reflecting the inhibitory effects on acid secretion and remained stable while treatment was continued. Gastrin values returned to pre-treatment levels, usually within 1 to 2 weeks after discontinuation of therapy.

Human gastric biopsy specimens from the antrum and the fundus from over 500 patients receiving rabeprazole or comparator treatment for up to 8 weeks have not detected changes in ECL cell histology, degree of gastritis, incidence of atrophic gastritis, intestinal metaplasia or distribution of H. pylori infection. In over 250 patients followed for 36 months of continuous therapy, no significant changes in findings present at baseline was observed.

Other Effects: Systemic effects of rabeprazole sodium in the CNS, cardiovascular and respiratory systems have not been found to date. Rabeprazole sodium given in oral doses of 20 mg for 2 weeks had no effect on thyroid function carbohydrate metabolism or circulating levels of parathyroid hormone cortisol, estrogen, testosterone, prolactin, cholecystokinin, secretin glucagon, follicle-stimulating hormone (FSH), luteinizing hormone (LH), renin, aldosterone or somatotrophic hormone.

Studies in healthy subjects have shown that rabeprazole sodium does not have clinically significant interactions with amoxicillin. Rabeprazole does not adversely influence plasma concentrations of amoxicillin or clarithromycin when co-administered for the purpose of eradicating upper gastrointestinal H. pylori infection.

Pharmacokinetic Properties:

Absorption: Rabeprazole sodium (PARIET®) is an enteric-coated (gastro resistant) tablet formulation of rabeprazole sodium. This presentation is necessary because rabeprazole is acid-labile. Absorption of rabeprazole therefore begins only after the tablet leaves the stomach. Absorption is rapid with peak plasma level of rabeprazole occurring approximately 3.5 hours after a 20 mg dose. Peak plasma concentrations (Cmax) of rabeprazole and AUC are linear over the dose range of 10 mg to 40 mg. Absolute bioavailability of an oral 20 mg dose (compared to intravenous administration) is about 52% due in large part to pre-systemic metabolism. Additionally, the bioavailability does not appear to increase with repeat administration. In healthy subjects, the plasma half-life is approximately one hour (range 0.7 to 1.5 hours), and the total body clearance is estimated to be 283±98mL/min. There was no clinically relevant interaction with food. Neither food nor the time of day of administration of the treatment affect the absorption of rabeprazole sodium.

Distribution: Rabeprazole is approximately 97% bound to human plasma proteins.

Metabolism and Excretion: Rabeprazole as is the case with other members of the proton pump inhibitor (PPI) class of compounds is metabolized through the cytochrome P450 (CYP450) hepatic drug metabolizing system. In vitro studies with human liver microsomes indicated that rabeprazole sodium is metabolized by isoenzymes of CYP450 (CYP2C19 and CYP34A). In these studies, at expected human plasma concentrations rabeprazole neither induces nor inhibits CYP34A; and although in vitro studies may not always be predictive of in vivo status, these findings indicate that no interaction is expected between rabeprazole and cyclosporine. In humans the thioether (M1) and carboxylic acid (M6) are the main plasma metabolites with the sulphone (M2), desmethyl thioether (M4) and mercapturic acid conjugate (M5) minor metabolites observed at lower levels. Only the desmethyl metabolite (M3) has a small amount of anti-secretory activity; but it is not present in plasma.

Following a single 20 mg14C labeled oral dose of rabeprazole sodium, no unchanged drug was excreted in the urine. Approximately 90% of the dose was eliminated in urine mainly as the two metabolites, a mercapturic acid conjugate (M5) and a carboxylic acid (M6), plus two unknown metabolites. The remainder of the dose was recovered in feces.

For the treatment of active duodenal ulcer, active benign gastric ulcer, anastomotic ulcer, erosive or ulcerative gastro-esophageal reflux disease (GERD), GERD maintenance, symptomatic GERD, eradication of Helicobacter pylori in patients with peptic ulcer diseases, Zollinger-Ellison Syndrome (ZES) and other pathological hypersecretory conditions and prevention of gastric and duodenal ulcer recurrences associated with low-dose aspirin therapy.

FULL PRESCRIBING AND SAFETY INFORMATION AVAILABLE

Manufactured by:
Bushu Pharmaceuticals Ltd. Misato Factory
950, Hiroki, Ohaza, Misato-machi, Kodama-gun,
Saitama-ken, Japan
Under License of Eisai Co., Ltd.

Packed by:
Bora Pharmaceuticals Co., Ltd.
No, 54 Gong-Yeh W, Rd, Guan-Tyan
District, Tainan City, Taiwan

Imported by:
HI-Eisai Pharmaceutical, Inc.
Unit 2, 22F Tower 6789
6789 Ayala Avenue, Makati City,
1226 Philippines
Tel. No.: 8887-1075

Suggested Retail Price	: Pariet 20mg - ₱ 101.00 Pariet 10mg - ₱ 76.00
FDA Registration No.	: Pariet 20mg - DR-XY25303 Pariet 10mg - DR-XY25304
Material Code	: PH-PR-CA-22C-01
Date of production materials	: March 2022

Reporting of Suspected Adverse Reactions

Please contact:
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Or Report to FDA Philippines: www.fda.gov.ph

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