SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF DRUG PRODUCT

Promto Tablets 20mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each enteric tablet contains:

Rabeprazole Sodium…. 20mg

3. PHARMACEUTICAL FORM

White colored, oblong shaped film coated tablets, engraved "CLARI 500" on one side and GETZ on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

PROMTO (Rabeprazole sodium) is indicated for the treatment of the following:

- Active duodenal ulcer.
- Active benign gastric ulcer.
- Symptomatic Erosive or Ulcerative Gastroesophageal Reflux Disease (GERD).
- Gastroesophageal Reflux Disease Long-term Management (GERD Maintenance).
- Zollinger-Ellison Syndrome.
- For the eradication of *Helicobacter pylori* in patients with peptic ulcer disease in combination with appropriate antibacterial therapeutic regimens.

4.2 Posology and method of administration

PROMTO (Rabeprazole sodium) tablets should be swallowed as whole and not crushed or chewed. The recommended adult dose of PROMTO (Rabeprazole sodium) is provided in the table below:

Disease	Adult dose	Course of therapy
Active duodenal ulcer	20mg daily in the morning. Some patients respond to 10mg dose	4 weeks. Few patients may require an additional 4 weeks therapy
Active benign gastric ulcer	20mg daily in the morning	6 weeks. Few patients may require an additional 6 weeks therapy.
Symptomatic Erosive or Ulcerative Gastroesophageal	20mg daily	4 - 8 weeks

Reflux Disease (GERD)		
Gastroesophageal Reflux Disease Long term Management (GERD Maintenance)	10 to 20mg daily	Depending upon patient's response
Zollinger-Ellison Syndrome	60mg daily as starting dose. Dose may be titrated based on patient need up to 120mg daily in 2 divided doses.	Treatment should continue as long as clinically indicated.
Eradication of *Helicobacter pylori*	[PROMTO 20mg + Clarithromycin 500mg + Amoxicillin 1gm] / twice daily	1 week

4.3 Contraindications

Rabeprazole sodium is contraindicated:
- In patients with known hypersensitivity to Rabeprazole or other substituted benzimidazoles or any component of this product.
- In pregnancy and during breast-feeding.

Rabeprazole sodium is not recommended for children, as there is no experience of its use in this group.

4.4 Special warnings and special precautions for use

- The possibility of malignancy should be excluded prior to commencing treatment with rabeprazole as symptomatic response to therapy with Rabeprazole sodium does not preclude the presence of gastric or esophageal malignancy. Patients on long-term treatment (particularly those treated for more than a year) should be kept under regular surveillance.

- Rabeprazole sodium should be used with caution in patients with severe hepatic dysfunction.

4.5 Interaction with other medicaments

Rabeprazole sodium produces a profound and long lasting inhibition of gastric acid secretion. An interaction with compounds whose absorption is pH dependent may occur. Co-administration of rabeprazole sodium with ketoconazole or itraconazole may result in a significant decrease in antifungal plasma levels. Therefore, individual patients may need to be monitored to determine if a dosage adjustment is necessary when ketoconazole or itraconazole are taken concomitantly with rabeprazole.

4.6 Pregnancy and Lactation

Rabeprazole Sodium is contraindicated in pregnancy and during breast-feeding.

4.7 Effects on ability to drive and use machine

It is unlikely that rabeprazole sodium would cause an impairment of driving performance or compromise the ability to use machinery.

4.8 Undesirable effects

Rabeprazole sodium is usually very well tolerated. However, following are the adverse events reported during therapy with rabeprazole sodium.

Common: Headache, diarrhea and nausea. Other adverse events were rhinitis, abdominal pain, asthenia, flatulence, pharyngitis, vomiting, non-specific pain/back pain, dizziness, flu like syndrome, infection, cough, constipation and insomnia.

Less frequent: Rash, myalgia, chest pain, dry mouth, dyspepsia, nervousness, somnolence, bronchitis, sinusitis, chills, eructation, leg cramps, urinary tract infection, arthralgia and fever.

Rare: Anorexia, gastritis, weight gain, depression, pruritus, vision or taste disturbances, stomatitis, sweating, leucocytosis, thrombocytopenia, neutropenia and leukopenia.

OVERDOSAGE

The maximum established exposure has not exceeded 60 mg twice daily, or 160 mg once daily. Effects are generally minimal, representative of the known adverse event profile and reversible without further medical intervention. No specific antidote is known. Rabeprazole sodium is extensively protein bound and is, therefore, not dialyzable. As in any case of overdose, treatment should be symptomatic and general supportive measures should be utilized.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

CLINICAL PHARMACOLOGY

Mechanism of Action

Rabeprazole sodium belongs to a new class of antisecretory compounds (substituted benzimidazole proton-pump inhibitor) that do not exhibit anticholinergic or histamine H_2-receptor antagonist properties, but suppress gastric acid secretion by inhibiting the gastric H^+/K^+ ATPase at the parietal cell. The effect is dose related and leads to the inhibition of both basal and stimulated acid secretion irrespective to the stimulus.

5.2 Pharmacokinetic properties

Absorption:

PROMTO (Rabeprazole sodium) is an enteric-coated formulation therefore, absorption begins only after the tablet leaves the stomach. Absorption is rapid, with peak plasma concentrations (C_{max}) of rabeprazole occurring approximately 3.5 hours (T_{max}) after a 20mg

dose. C_{max} and AUC of rabeprazole are linear over the dose range of 10mg to 40mg. Absolute bioavailability of an oral 20mg dose is about 52%. The plasma half-life is approximately 1 hour. 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:
Following absorption, rabeprazole sodium undergoes extensive hepatic metabolism. The resulting metabolites have no significant antisecretory activity.

Excretion:
Approximately 90% of the dose was eliminated in the urine primarily as metabolites. The remainder of the dose was recoverable in the feces.

Special Populations:
Renal Insufficiency
In patients with stable, end-stage, renal failure requiring maintenance hemodialysis (creatinine clearance $\leq$ 5mL/min/1.73m^2), the disposition of rabeprazole was very similar to that in healthy volunteers. The AUC and the C_{max} in these patients was about 35% lower than the corresponding parameters in healthy volunteers. The mean half-life of rabeprazole was 0.82 hours in healthy volunteers, 0.95 hours in patients during hemodialysis and 3.6 hours post dialysis. The clearance of the drug in patients with renal disease requiring maintenance hemodialysis was approximately twice that in healthy volunteers.

Hepatic Insufficiency
Following a single 20mg dose of rabeprazole to patients with chronic mild to moderate hepatic impairment the AUC doubled and there was a 2-3 fold increase in half-life of rabeprazole compared to the healthy volunteers. However, following a 20mg dose daily for 7 days the AUC had increased to only 1.5-fold and the C_{max} to only 1.2-fold. The half-life of rabeprazole in patients with hepatic impairment was 12.3 hours compared to 2.1 hours in healthy volunteers. The pharmacodynamic response (gastric pH control) in the two groups was clinically comparable.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Light Magnesium Oxide, Mannitol, Croscarmellose Sodium, Hydroxypropyl Cellulose (Klucel-EXF), Microcrystalline Cellulose (Avicel PH 102), Magnesium Stearate, Purified Talc, Isopropyl Alcohol, Dichloromethane, Hypromellose (HPMC 5CPS), Macrogols (P.E.G 6000), Acryl-Eze White, Opadry II Orange 85G43136, Purified Water & Purified Talc

6.2 Incompatibilities

None

6.3 Shelf-life

2 Years
The expiration dates refer to the product correctly stored in the required conditions.

6.4 Special precautions for storage

Store below 30ºC
Protect from sunlight & moisture.
The expiration date refers to the product correctly stored at the required conditions.

6.5 Nature and contents of container

Promto (Rabeprazole Sodium) Tablets 20mg are available in Alu-Alu blister pack of 1 x 10's tablets.

6.6 Instructions for use/handling

- To be sold on prescription of a registered medical practitioner only.
- Keep out of the reach of children.

7. MARKETING AUTHORISATION HOLDER

Getz Pharma (Pvt.) Limited
29-30/27, Korangi Industrial Area Karachi 74900, Pakistan
Tel: (92-21) 111 111 511
Fax: (92-21) 505 7592

8. PRODUCT REGISTRATION NUMBER

005127-EX

9. DATE OF PRODUCT REGISTRATION ISSUED

February 17, 2016