1. NAME OF THE MEDICINAL PRODUCT

Rabeprazole Sodium Tablets 20 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Label claim:

Each enteric coated tablet contains

Rabeprazole Sodium 20 mg

(Batch Size: 100000 Tablets)

Sr. No.	Material Name	Spc.	Function	Theo. qty. Per tab. (mg)	OA %	Actual qty. Per tab. (mg)	Actual qty. Per Batch (Kg)
MIXING							
1	Mannitol	BP	Diluent	52.700	---	52.700	5.270
2	Sodium Carbonate	BP	Preservative	10.000	---	10.000	1.000
3	Crospovidone	USP	Disintegrant	16.000	---	16.000	1.600
4	$Rabeprazole Sodium	BP	Active	20.000	---	20.000	2.000
5	Heavy Magnesium Oxide	BP	Alkaliser	30.000	---	30.000	3.000
WET GRANULATION							
6	Hypromellose	USP	Binder	3.500	---	3.500	0.350
7	#Purified Water	BP	Solvent	0.030 ml	---	0.030 lit	3.000 Lit.
8	Sodium Lauryl Sulphate	BP	Disintegrant	1.800	---	1.800	0.180
LUBRICATION							
9	Magnesium Stearate	BP	Lubricant	4.000	---	4.000	0.400
10	Purified Talc	BP	Antiadherent	2.000	---	2.000	0.200
11	Crospovidone	USP	Disintegrant	17.000	---	17.000	1.700
COMPRESSED WEIGHT						**157.000 mg**	**15.700 Kg**
ENTERIC COATING							
12	@Easy Coat ECM (Sunset Yellow)	IH	Coating Agent	10.000	20	12.000	1.200
13	@#Isopropyl Alcohol	BP	Solvent	0.0863 ml	20	0.1036 ml	10.360 Lit.
14	@#Dichloromethane	BP	Solvent	0.0269 gm	20	0.0323 gm	3.230
TOTAL WEIGHT						**167.000 mg**	**16.900 Kg**

Note: $Qty. of active materials shall be vary with assay and LOD.

(Assay considered is 100% and LOD 0%).

Final qty. shall be compensated with Mannitol.

#Quantity of these materials will not be calculated in total weight of tablet.

@Overages of coating materials are added to compensate the loss during coating.

Average weight of coated tablet after coating should be achieved approximately 6.37%

USP - United States Pharmacopeia, BP - British Pharmacopeia & IH – In-House

3. PHARMACEUTICAL FORM

Oral Solid dosage (Oral Tablet)

Description: Orange coloured, round shaped, biconvex, enteric coated tablet plain on both sides.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Rabeprazole Sodium Tablets are indicated for the treatment of:

- Active duodenal ulcer
- Active benign gastric ulcer
- Symptomatic erosive or ulcerative gastro-oesophageal reflux disease (GORD).
- Gastro-Oesophageal Reflux Disease Long-term Management (GORD Maintenance)
- Symptomatic treatment of moderate to very severe gastro-oesophageal reflux disease (symptomatic GORD)
- Zollinger Ellison Syndrome

4.2 Posology/Dosage and method of administration

Posology

Adults/elderly:

Active Duodenal Ulcer and Active Benign Gastric Ulcer: The recommended oral dose for both active duodenal ulcer and active benign gastric ulcer is 20 mg to be taken once daily in the morning.

Symptomatic treatment of moderate to very severe gastro-oesophageal reflux disease (symptomatic GORD): 10 mg once daily in patients without oesophagitis. If symptom control has not been achieved during four weeks, the patient should be further investigated. Once symptoms have resolved, subsequent symptom control can be achieved using an on-demand regimen taking 10 mg once daily when needed.

Zollinger-Ellison Syndrome: The recommended adult starting dose is 60 mg once a day. The dose may be titrated upwards to 120 mg/day based on individual patient needs. Single daily doses up to 100 mg/day may be given. 120 mg dose may require divided doses, 60mg twice daily. Treatment should continue for as long as clinically indicated.

For indications requiring once daily treatment Rabeprazole Sodium tablets should be taken in the morning, before eating; and although neither the time of day nor food intake was shown to have any effect on Rabeprazole sodium activity, this regimen will facilitate treatment compliance. Patients should be cautioned that the Rabeprazole Sodium tablets should not be chewed or crushed, but should be swallowed whole.

Children: Rabeprazole Sodium is not recommended for use in children, as there is no experience of its use in this group

Method of administration

Oral use

4.3 Contraindications

Rabeprazole Sodium is contra-indicated in patients with known hypersensitivity to Rabeprazole sodium, substituted Benzimidazoles or to any excipient used in the formulations. Rabeprazole Sodium is contra-indicated in pregnancy and during breastfeeding.

4.4 Special warnings and precautions for use

Patients on long-term treatment should be kept under regular surveillance.

Patients should be cautioned that Rabeprazole Sodium Tablets should not be chewed or crushed, but should be swallowed whole. Co-administration of atazanavir with Rabeprazole is not recommended.

4.5 Interaction with other medicinal products and other forms of interaction

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.

Antacids were used concomitantly with the administration of Rabeprazole and, in a specific drug-drug interaction study, no interaction with liquid antacids was observed.

Co-administration of atazanavir 300 mg/ritonavir 10 mg with omeprazole (40 mg once daily) or atazanavir 400 mg with lansoprazole (60 mg once daily) to healthy volunteers resulted in a substantial reduction in atazanavir exposure. The absorption of atazanavir is pH dependent. Although not studied, similar results are expected with other proton pump inhibitors. Therefore PPIs, including Rabeprazole, should not be co-administered with atazanavir.

4.6 Fertility, pregnancy and lactation

Pregnancy: There are no data on the safety of Rabeprazole in human pregnancy. Reproduction studies performed in rats and rabbits have revealed no evidence of impaired fertility or harm to the foetus due to Rabeprazole sodium, although low foeto-placental transfer occurs in rats. Rabeprazole Tablets is contraindicated during pregnancy.

Breastfeeding: It is not known whether Rabeprazole sodium is excreted in human breast milk. No studies in lactating women have been performed. Rabeprazole sodium is however excreted in rat mammary secretions. Therefore Rabeprazole Tablets must not be used during breast feeding.

4.7 Effects on ability to drive and use machines

Based on the pharmacodynamics properties and the adverse events profile, it is unlikely that Rabeprazole Tablets would cause an impairment of driving performance or compromise the ability to use machinery. If however, alertness is impaired due to somnolence, it is recommended that driving and operating complex machinery be avoided.

4.8 Undesirable effects

The most commonly reported adverse drug reactions were headache, diarrhoea, abdominal pain, asthenia, flatulence, rash and dry mouth. The majority of adverse events experienced during clinical studies were mild or moderate in severity and transient in nature.

4.9 Overdose

The maximum established exposure has not exceeded 60mg 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 dialysable. As in any case of overdose, treatment should be symptomatic and general supportive measures should be utilised.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamics properties

Mode of Action

Rabeprazole sodium belongs to the class of anti-secretory compounds, the substituted benzimidazoles, suppress gastric acid secretion by the specific inhibition of the H+/K+- ATPase enzyme. Rabeprazole is converted to the active sulphonamide form through protonation and it subsequently reacts with the available cysteines on the proton pump.

5.2 Pharmacokinetic properties

Absorption: Rabeprazole sodium is enteric coated 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 levels of Rabeprazole occurring approximately 3.5 hours after a 20 mg dose. Peak plasma concentration (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 is about 52 % due in large part of pre-systemic metabolism. In healthy subjects the plasma half-life is approximately one hour, and the total body clearance is estimated to be 283 ± 98 ml/min.

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

Metabolism and excretion: Rabeprazole sodium 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-metabolising system. In these studies, at expected human plasma concentrations Rabeprazole neither induces nor inhibits CYP3A4; 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 cyclosporin. In humans the thioether (MI) and carboxylic acid (M6) are the main plasma metabolites with the sulphone (M2), desmethyl- thioether (M4) and mercapturic acid (M6) are the main plasma metabolites observed at lower levels.

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 faeces.

5.3 Preclinical safety data

Non-clinical effects were observed only at exposures sufficiently in excess of the maximum human exposure that make concerns for human safety negligible in respect of animal data.

Studies on mutagenicity gave equivocal results. Tests in mouse lymphoma cell line were positive, but *in vivo* micronucleus and *in vivo* and *in vitro* DNA repair tests were negative. Carcinogenicity studies revealed no special hazard for humans.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Mannitol BP
Sodium Carbonate BP
Crospovidone USP
Heavy Magnesium Oxide BP
Hypromellose USP
Purified Water BP
Sodium Lauryl Sulphate BP
Magnesium Stearate BP
Purified Talc BP
Easy Coat ECM (Sunset Yellow) IH
Isopropyl Alcohol BP
Dichloromethane BP

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage

Store below 30°C.
Protect from light and moisture.

6.5 Nature and contents of container

1x10 Alu-Alu blister pack: 10 Tablets packed in Alu-Alu blister pack and such 1 blister is to be packed in carton along with insert.
3x10 Alu-Alu blister pack: 10 Tablets packed in Alu-Alu blister pack and such 3 blister is to be packed in carton along with insert.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. APPLICANT/HOLDER OF CERTIFICATE OF PRODUCT REGISTRATION

Pacmai International Limited

8, Alhaji Yusuf Adebayo Street, Olodi Apapa, Lagos.

8. DRUG PRODUCT MANUFACTURER

Corona Remedies Pvt. Ltd.

Village Jatoli, Post Office Oachghat,

Tehsil Solan, Distt. Solan (H.P.) – 173 223

Fax: +079-40233999

Email: info@coronaremedies.com

9. NAFDAC REGISTRATION NUMBER(S)

NAFDAC REG. NO.: B4-8863