SUMMARIES OF PRODUCT CHARACTERISTICS (SmPC)

1. Name of the finished pharmaceutical product

Dom R Capsules

Enteric coated Rabeprazole Sodium and Domperidone SR Capsules

2. Qualitative and quantitative composition

Each hard gelatin capsule contains

Rabeprazole Sodium 20 mg

(as enteric coated pellets)

Domperidone BP 30 mg

(as sustained release pellets)

Excipients Q.S.

Approved colours used in empty capsule shell

3. Pharmaceutical form

Oral capsule

4. Clinical particulars

1. Therapeutic indications

Enteric coated Rabeprazole Sodium 20 mg and Domperidone 30 mg SR Capsules are indicated forthe 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, In combination with appropriate antibacterial therapeutic regimens forthe eradication of Helicobacter pylori in patients with peptic ulcer disease.

2. Posology and method of administration

Adults: Enteric coated Rabeprazole Sodium 20 mg and Domperidone 30 mg SR Capsule up to two times a day or as directed by Physician.

Children: Enteric coated Rabeprazole Sodium 20 mg and Domperidone 30 mg SR Capsules are not recommended for use in children due to a lack of data on safety and efficacy.

3. Contraindications

Hypersensitivity to the active substance or to any of the excipients used in the formulation, Prolactin-releasing pituitary tumour (prolactinoma), in patients with moderate or severe hepatic impairment, Co-administration with QT-prolonging drugs, Co-administration with potent CYP3A4 inhibitors, Pregnancy and Breastfeeding.

4. Special warnings and special precautions for use

Rabeprazole:

Symptomatic response to therapy with Rabeprazole sodium does not preclude the presence of gastric or oesophageal malignancy, therefore the possibility of malignancy should be excluded prior to commencing treatment with capsule. A risk of cross-hypersensitivity reactions with other proton pump inhibitor or substituted benzimidazoles cannot be excluded.

Patients should be cautioned that Enteric coated Rabeprazole Sodium 20 mg and Domperidone 30 mg SR Capsules should not be chewed or crushed, but should be swallowed whole.

Enteric coated Rabeprazole Sodium 20 mg and Domperidone 30 mg SR Capsule is not recommended for use in children due to a lack of data on safety and efficacy.

There have been post marketing reports of blood dyscrasias (thrombocytopenia and neutropenia). In the majority of cases where an alternative aetiology cannot be identified, the events were uncomplicated and resolved on discontinuation of Rabeprazole.

Co-administration of Atazanavir with Rabeprazole is not recommended.

Decreased gastric acidity due to any means including proton pump inhibitors, increases gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with proton pump inhibitors may lead to slightly increased risk of gastrointestinal infections such as Salmonella and Campylobacter.

Domperidone:

Renal impairment - The elimination half-life of Domperidone is prolonged in severe renal impairment.

Cardiovascular effects: Domperidone has been associated with prolongation of the QT interval on the electrocardiogram. During post-marketing surveillance, there have been very rare cases of QT prolongation and torsades de pointes in patients taking Domperidone. These reports included patients with confounding risk factors, electrolyte abnormalities and concomitant treatment which may have been contributing factors.

5. Interaction with other FPPS and other forms of interaction

Rabeprazole:

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.

In clinical trials, 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.

Domperidone:

Concomitant use of the following substances is contraindicated

QTc-prolonging medicinal products

Anti-arrhythmics class IA (e.g., disopyramide, hydroquinidine, quinidine), Anti-arrhythmics class III (e.g., amiodarone, dofetilide, dronedarone, ibutilide, sotalol), Certain antipsychotics (e.g., haloperidol, pimozide, sertindole), Certain antidepressants (e.g.,

citalopram, escitalopram), Certain antibiotics (e.g., erythromycin, levofloxacin, moxifloxacin, spiramycin), Certain antifungal agents (e.g., pentamidine), Certain antimalarial agents (in particular halofantrine, lumefantrine), Certain gastro-intestinal medicines (e.g., cisapride, dolasetron, prucalopride), Certain antihistaminics (e.g., mequitazine, mizolastine), Certain medicines used in cancer (e.g., toremifene, vandetanib, vincamine), Certain other medicines (e.g., bepridil, diphemanil, methadone), Potent CYP3A4 inhibitors (regardless of their QT prolonging effects), i.e. protease inhibitors, systemic azole antifungals, some macrolides (erythromycin, clarithromycin and telithromycin).

Concomitant use of the following substances is not recommended

Moderate CYP3A4 inhibitors i.e. diltiazem, verapamil and some macrolides.

Concomitant use of the following substances requires caution in use

Caution with bradycardia and hypokalaemia-inducing drugs, as well as with the following macrolides involved in QT-interval prolongation: azithromycin and roxithromycin (clarithromycin is contra-indicated as it is a potent CYP3A4 inhibitor).

The above list of substances is representative and not exhaustive.

Opioids may antagonise the effects of Domperidone on gastric emptying.

6. Use in Pregnancy and lactation

Rabeprazole:

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. Enteric coated Rabeprazole Sodium 20 mg and Domperidone 30 mg SR Capsule is contraindicated during pregnancy.

Lactation: 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 Enteric coated Rabeprazole Sodium 20 mg and Domperidone 30 mg SR Capsule must not be used during breastfeeding.

SUMMARIES OF PRODUCT CHARACTERISTICS (SmPC)

Domperidone:

Pregnancy: There are limited post-marketing data on the use of Domperidone in pregnant women. A study in rats has shown reproductive toxicity at a high, maternally toxic dose. The potential risk for humans is unknown. Therefore, Domperidone should only be used during pregnancy when justified by the anticipated therapeutic benefit.

Lactation: Domperidone is excreted in human milk and breast-fed infants receive less than 0.1 % of the maternal weight-adjusted dose. Occurrence of adverse effects, in particular cardiac effects cannot be excluded after exposure via breast milk. A decision should be made whether to discontinue breast-feeding or to discontinue/abstain from Domperidone therapy taking into account the benefit of breastfeeding for the child and the benefit of therapy for the woman. Caution should be exercised in case of QTc prolongation risk factors in breast-fed infants.

7. Undesirable effects

Neutropenia, Leucopenia, Hypersensitivity, Anorexia, Insomnia, Nervousness, Headache, Dizziness, Cough, Pharyngitis, Rhinitis, Diarrhea, Vomiting, Nausea, Abdominal pain, Constipation, Flatulence, Rash, Back pain, Asthenia, Influenza like illness, Allergic reaction, increased prolactin levels, agitation, nervousness, extrapyramidal side effects, convulsion, somnolence, headache, gastro-intestinal disorders including very rare transient intestinal cramps, very rare; diarrhea, breast pain

8. Overdose

Rabeprazole

Experience to date with deliberate or accidental overdose is limited. 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 dialysable. As in any case of overdose, treatment should be symptomatic and general supportive measures should be utilized.

Domperidone

Symptoms: Overdose has been reported primarily in infants and children. Symptoms of overdosage may include agitation, altered consciousness, convulsion, disorientation, somnolence and extra pyramidal reactions.

Treatment: There is no specific antidote to Domperidone, but in the event of overdose, standard symptomatic treatment should be given immediately. Gastric lavage as well as the administration of activated charcoal, may be useful. ECG monitoring should be undertaken, because of the possibility pf QT prolongation. Close medical supervision and supportive therapy is recommended.

Anticholinergic, Anti-Parkinson drugs may be helpful in controlling extrapyramidal reactions

SUMMARIES OF PRODUCT CHARACTERISTICS (SmPC)

5. Pharmacological properties

5.1 Pharmacodynamic properties

Rabeprazole:

Rabeprazole sodium belongs to the class of anti-secretory compounds, the substituted benzimidazoles that do not exhibit anticholinergic or H2 histamine antagonist properties, but suppress 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.

Domperidone:

Domperidone is a dopamine antagonist with anti-emetic properties Domperidone does not readily cross the blood-brain barrier. In Domperidone users, especially in adults, extrapyramidal side effects are very rare, but Domperidone promotes the release of prolactin from the pituitary. Its anti-emetic effect may be due to a combination of peripheral (gastrokinetic) effects and antagonism of dopamine receptors in the chemoreceptor trigger zone, which lies outside the blood-brain barrier in the area postrema. Animal studies, together with the low concentrations found in the brain, indicate a predominantly peripheral effect of Domperidone on dopamine receptors.

5.2. Pharmacokinetic properties

Rabeprazole:

Absorption: It is an enteric-coated (gastro-resistant) Pellets in capsule formulation of Rabeprazole sodium. This presentation is necessary because Rabeprazole is acid-labile. Absorption of Rabeprazole therefore begins only after the capsule leaves the stomach. Absorption is rapid, with peak plasma levels of Rabeprazole occurring approximately 3.5 hours after a 20 mg dose.

Peak plasma concentrations (CmJ of Rabeprazole and AUC are linear over the dose range of 10 mg to 40 mg. 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 ± 98 ml/min. There was no clinically relevant interaction with food. Neitherfood northe time of day of administration of the treatment affects the absorption of Rabeprazole sodium.

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

Metabolism and Excretion: Rabeprazole sodium is metabolised through the cytochrome P450 (CYP450) hepatic drug metabolizing system. In vitro studies with human liver microsomes indicated that Rabeprazole sodium is metabolised by isoenzymes of CYP450 (CYP2C19 and CYP3A4). 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 cyclosporine.

Domperidone:

Absorption: Domperidone is rapidly absorbed after oral administration with peak plasma concentrations at approximately 1 hr after dosing. The Cmax and AUC values of Domperidone increased proportionally with dose in the 10 mg to 20 mg dose range. A 2- to 3-fold accumulation of Domperidone AUC was observed with repeated four times daily (every 5 hr) dosing of Domperidone for 4 days. The low absolute bioavailability of oral Domperidone (approximately 15%) is due to an extensive first-pass metabolism in the gut wall and liver.

Distribution: Oral Domperidone does not appearto accumulate or induce its own metabolism; a peak plasma level after 90 minutes of 21 ng/ml after two weeks oral administration of 30 mg per day was almost the same as that of 18 ng/ml after the first dose. Domperidone is 91 -93% bound to plasma proteins. Distribution studies with radiolabeled drug in animals have shown wide tissue distribution, but low brain concentration. Small amounts of drug cross the placenta in rats.

Metabolism: Domperidone undergoes rapid and extensive hepatic metabolism by hydroxylation and N-dealkylation in vitro metabolism experiments with diagnostic inhibitors revealed that CYP3A4 is a major form of cytochrome P-450 involved in the N-dealkylation of Domperidone whereas CYP3A4, CYP1A2 AND CYP2E1 are involved in Domperidone aromatic hydroxylation.

Excretion: Urinary and faecal excretions amount to 31 and 66% of the oral dose respectively, the proportion of the drug excreted unchanged is small (10% of faecal excretion and approximately 1 % of urinary excretion). The plasma half-life after a single oral dose is 7-9 hours in healthy subjects but is prolonged in patients with severe renal insufficiency

5.3. Preclinical safety data: None

6. Pharmaceutical particulars

1. List of excipients

Dummy Pellets

2. Incompatibilities: Not applicable

3. In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products: This medicinal product must not be mixed with other medicinal products.

4. Shelf life: 24 months

5. Special precautions for storage:

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

Keep the medicine out of reach of children.

6. Special precautions for usage / preparation before use: No special requirement.

7. Packing Style: 10 capsules are packed in Alu/Alu Blister pack, such 3 blisters are packed in carton along with insert.

8. Manufactured By

Corona Remedies Pvt. Ltd.

Village Jatoli, Post Office- Ochghat,

Tehsil Solan, Dist. Solan (H.P.), Solan, India