SUMMARIES OF PRODUCT CHARACTERISTICS (SmPC)

1. Name of the finished pharmaceutical product

Ulpan-40 ER

(Pantoprazole Capsules)

2. Qualitative and quantitative composition

Each hard gelatin capsule contains:

Pantoprazole Sodium Sesquihydrate BP

Equivalent to Pantoprazole 40 mg

(as enteric coated pellets)

Excipients Q.S.

Approved colours used in empty capsule shell.

3. Pharmaceutical form

Oral Capsules

4. Clinical particulars

a. Therapeutic indications

For treatment of Zollinger-Ellison syndrome, Gastroesophageal reflux disease (GERD), Gastric and duodenal ulcers, H. pylori associated ulcers and pathological hypersecretory conditions.

b. Posology and method of administration

One capsule daily or use as directed by the Physician.

Method of administration: Capsule should not be chewed or crushed, and should be swallowed whole, 1 hour before meal with some water.

c. Contraindications

Hypersensitivity to the active substance.

d. Special warnings and special precautions for use

Hepatic Impairment: In patients with severe liver impairment, the liver enzymes should be monitored regularly during treatment with Pantoprazole, particularly on long-term use.

Long term treatment: In long-term treatment, especially when exceeding a treatment period of 1 year, patients should be kept under regular surveillance.

Gastrointestinal infections caused by bacteria: Treatment with Pantoprazole may lead to a slightly increased risk of gastrointestinal infections caused by bacteria such as Salmonella and Campylobacter and C. difficult.

Hypomagnesaemia: Severe hypomagnesaemia has been reported in patients treated with PPIs like Pantoprazole for at least three months, and in most cases for a year.

Bone fractures: Proton pump inhibitors, especially if used in high doses and over long durations (>1 year), may modestly increase the risk of hip, wrist and spine fracture.

e. Interaction with other FPPS and other forms of interaction

HIV medications (Atazanavir): Co-administration of Atazanavir and other HIV medications whose absorption is pH-dependent with proton-pump inhibitors might result in a substantial reduction in the bioavailability and efficacy.

Methotrexate: Concomitant use of high dose methotrexate (e.g. 300 mg) and proton-pump inhibitors has been reported to increase methotrexate levels in some patients.

Other interactions studies: Pantoprazole is extensively metabolized in the liver via the cytochrome P450 enzyme system. Interaction studies with drugs also metabolized with these pathways, like carbamazepine, diazepam, glibenclamide, nifedipine, and an oral contraceptive containing levonorgestrel and Ethinyl estradiol did not reveal clinically significant interactions.

f. Use in Pregnancy and lactation

Pregnancy: There are no adequate data from the use of Pantoprazole in pregnant women. Pantoprazole should not be used during pregnancy unless clearly necessary.

Breast-feeding: Excretion of Pantoprazole into human milk has been reported. Therefore a decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with

Pantoprazole should be made taking into account the benefit of breast- feeding to the child and the benefit of Pantoprazole therapy to women.

g. Undesirable effects

The most commonly reported ADRs are diarrhoea and headache.

Uncommon: Sleep disorders, Headche, Dizziness, Diarrhoea, Abdominal distension and bloating, Constipation, Dry mouth, Abdominal pain and discomfort, Liver enzymes increased (trnsaminases, γ-GT), Rash/exanthema/eruption, Pruritus, Asthenia, fatigue and malaise.

Rare: Agranulocytosis, Hypersensitivity, Hyperlipidaemias and lipid increases (triglycerides, cholesterol), Weight changes, Angioedema, Arthralgia, Myalgia, Gynaecomastia, Body temperature increased, edema peripheral

Very Rare: Thrombocytopenia, Leukopenia, Pancytopenia, Disorientation (and all aggravations)

h. Overdose

There are no known symptoms of overdose in humans. In the case of overdose with clinical signs of intoxication, apart from symptomatic and supportive treatment, no specific therapeutic recommendations can be made.

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5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Proton pump inhibitors

ATC code: A02BC02

Mechanism of action: Pantoprazole is a substituted benzimidazole which inhibits the secretion of hydrochloric acid in the stomach by specific blockade of the proton pumps of the parietal cells. Pantoprazole is converted to its active form in the acidic environment in the parietal cells where it inhibits the H+, K+-ATPase enzyme. As with other proton pump inhibitors and H2 receptor inhibitors, treatment with Pantoprazole reduces acidity in the stomach and thereby increases gastrin in proportion to the reduction in acidity.

5.2. Pharmacokinetic properties

Absorption: Pantoprazole is rapidly absorbed and the maximal plasma concentration is achieved even after one single 40 mg oral dose. On average at about 2.5 h p.a. the maximum serum concentrations of about 2 - 3 µg/ml are achieved, and these values remain constant after multiple administration.

Distribution: Pantoprazole's serum protein binding is about 98 %. Volume of distribution is about 0.15 l/kg

Metabolism and Elimination: The substance is almost exclusively metabolized in the liver. Terminal half-life is about 1 hour and clearance is about 0.1 l/h/kg. Renal elimination represents the major route of excretion (about 80 %) for the metabolites of Pantoprazole; the rest is excreted with the faeces.

5.3. Preclinical safety data

Preclinical data reveal no special hazard to humans based on conventional studies of safety pharmacology, repeated dose toxicity and genotoxicity. In the two-year carcinogenicity studies in rats neuroendocrine neoplasms were found. In addition, squamous cell papillomas were found in the fore stomach of rats. The mechanism leading to the formation of gastric carcinoids by substituted benzimidazoles has been carefully investigated and allows the conclusion that it is a secondary reaction to the massively elevated serum gastrin levels occurring in the rat during

chronic high-dose treatment. In the two-year rodent studies an increased number of liver tumours was observed in rats and in female mice and was interpreted as being due to pantoprazole's high metabolic rate in the liver.

A slight increase of neoplastic changes of the thyroid was observed in the group of rats receiving the highest dose (200 mg/kg). The occurrence of these neoplasms is associated with the pantoprazole-induced changes in the breakdown of thyroxine in the rat liver. As the therapeutic dose in man is low, no harmful effects on the thyroid glands are expected.

In animal reproduction studies, signs of slight fetotoxicity were observed at doses above 5 mg/kg. Investigations revealed no evidence of impaired fertility or teratogenic effects. Penetration of the placenta was investigated in the rat and was found to increase with advanced gestation. As a result, concentration of pantoprazole in the foetus is increased shortly before birth.

6. Pharmaceutical particulars

a. List of excipients

- Dummy Pellets (Size 16120)
- E.H.G. Green/CT (Size"2") capsules

b. Incompatibilities: Not applicable

c. 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.

d. Shelf life: 24 months

e. Special precautions for storage:

Store below 30ºC. Protect from light and moisture.

Keep the medicine out of reach of children.

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

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

8. Manufactured By

Corona Remedies Pvt. Ltd.

Village Jatoli, Post Office- Ochghat,

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