## 1.3 Product Information

### 1.3.1 Summary of Product Characteristics

Summary of product characteristic is attached.

# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. Trade Name of Medicinal Product

ZAPACID CAPSULES 30 mg
(Lansoprazole Capsules)

## 2. Qualitative and Quantitative Composition

| Ingredients | mg/ Capsules | Active / Inactive | Pharma-copoeial Reference | Function |
|---|---|---|---|---|
| Lansoprazole pellets 8.5% w/w | 363.00* | Active | IH | Proton Pump Inhibitor |
| EG capsule Orange/White (OR 155/WH004) printed Zapacid & 30 | 1 No. | Capsule shell | IH | Capsule shell |

* includes 2.85% overages

## 3. Pharmaceutical Form

Oral Capsules

## 4. Clinical Particulars

### 4.1 Therapeutic Indications

- Treatment of active duodenal ulcers.
- Maintenance of healed duodenal ulcers.
- Treatment of active benign gastric ulcers.
- Maintenance of healed gastric ulcers.
- Gastroesophageal Reflux Disease (GERD).
- Maintenance of Healing of Erosive Oesophagitis.
- Acid-Related Dyspepsia.
- NSAID-Associated Benign Gastric/Duodenal Ulcers and Relief of Symptoms.
- H. Pylori eradication (in combination with other drugs).
- Zollinger-Ellison Syndrome.

### 4.2 Posology and Method of Administration

- The dose and duration of therapy depends on the severity of disease and the patient's response. Some patients may require treatment schedules to be repeated.
- Treatment of active duodenal ulcers: Zapacid 30 mg once daily for 4 weeks.
- Maintenance of healed duodenal ulcers: Zapacid 15 mg once daily.
- Treatment of active benign gastric ulcers: Zapacid 30 mg once daily for up to 8 weeks.
- Maintenance of healed gastric ulcers: Zapacid 15 mg once daily.
- Gastroesophageal reflux disease (GERD): Zapacid 30 mg once daily for 4 weeks.
- Maintenance of healing of erosive oesophagitis: Zapacid 15 mg once daily.

- Acid-related dyspepsia: Zapacid 15 mg or 30 mg for 2-3 weeks.
- NSAID-associated benign gastric/duodenal ulcers and relief of symptoms: Zapacid 15 mg or 30mg once daily for 4-8 weeks.
- H. pylori eradication: Zapacid 30 mg b.i.d. in combination anyone of the following regimens (or appropriate alternatives): clarithromycin 250/500 mg b.i.d. plus metronidazole 400 mg b.i.d./t.i.d. for 7 days, or amoxicillin 1 gm b.i.d./500 mg t.i.d. plus metronidazole 400 mg b.i.d./t.i.d. for 7 days.
- Zollinger-Ellison Syndrome: Zapacid 60-120 mg (or more) in daily divided doses.
- Zapacid Capsules should be taken before meals.
- Neither the capsules nor the pellets should be chewed or crushed.

**4.3 Contraindications**

Lansoprazole Capsules are contraindicated in patients with known hypersensitivity to any component of the formulation.

**4.4 Special Warnings and Special Precautions for Use**

Patients who do not respond within 4 weeks or relapse quickly should be thoroughly investigated.

When gastric ulcer is suspected, the possibility of malignancy should be excluded before therapy with Lansoprazole is instituted, as treatment with this drug may alleviate symptoms and delay diagnosis.

Use in pregnancy: Pregnancy category – B. There are no adequate or well-controlled studies in pregnant women. Therefore, Lansoprazole should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Use in nursing mothers: It is not known whether Lansoprazole is excreted in human milk. Lansoprazole should not be given to nursing mothers unless its use is considered essential.

Use in children: Safety and effectiveness in children have not been established.

Use in elderly patients: The initial dosing regimen need not be altered for elderly patients, but subsequent doses higher than 30 mg per day should not be administered unless additional gastric acid suppression is necessary.

Use in renally impaired patients: No dosage modification is required.

Use in hepatically impaired patients: The initial dosing regimen need not be altered for patients with mild liver disease, but for patients with moderate impairment, doses higher than 30 mg per day should not be administered unless there are compelling clinical indications.

**4.5 Interaction with Other Medicinal Products and Other Forms of Interaction**

Lansoprazole does not have clinically significant interactions with Warfarin, Indomethacin, aspirin, ibuprofen, Phenytoin, prednisone, antacids or diazepam in healthy subjects. Lansoprazole administered concomitantly with Theophylline causes a minor increase (10%) in the clearance of Theophylline. Sucralfate, if co-prescribed, should be taken at least 30 minutes after Lansoprazole. Lansoprazole may, theoretically, interfere with the absorption of drugs where gastric pH is an important determinant of bioavailability (e.g., Ketoconazole, Ampicillin esters, and iron salts digoxin).

## 4.6 Pregnancy and Lactation

**Use in Pregnancy:**

Pregnancy category – B. There are no adequate or well-controlled studies in pregnant women. Therefore, Lansoprazole should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**Use in nursing mothers:**

It is not known whether Lansoprazole is excreted in human milk. Lansoprazole should not be given to nursing mothers unless its use is considered essential.

## 4.7 Effects on Ability to Drive and Use Machines

Not known

## 4.8 Undesirable Effects

The most frequent adverse effects reported in the European short-term studies were diarrohea (3.3%), Laboratory test abnormalities (2.3%), headache (1.5%), constipation 1.2%, asthenia (1.1%), dizziness (1.1%), and abdominal pain (1.0%). The most frequent adverse effects reported in the Asian short-term studies were unspecified laboratory test abnormalities (7.3%), esosinophilia (1.0%) and increased SGPT (1.0%).

## 4.9 Overdose

In one case of overdose, a patient consumed 600 mg of Lansoprazole with no adverse reaction. Lansoprazole is extensively protein bound and is not readily dialyzable. Treatment should be symptomatic and supportive.

## 5. Pharmacological Properties

### 5.1 Mode of Action

Lansoprazole suppresses gastric acid secretion by selective inhibition of the parietal cell membrane enzyme $H^+/K^+$ ATPase (the proton pump). Both centrally and peripherally mediated gastric and secretion is inhibited.

### 5.2 Pharmacokinetic Properties

Zapacid delayed-release capsules contain an enteric coated granule formulation of Lansoprazole. Absorption of Lansoprazole begins only after the granules leave the stomach.

**Absorption**

The absorption of Lansoprazole is rapid, with mean $C_{max}$ occurring approximately 1.7 hours after oral dosing, and relatively complete with absolute bioavailability over 80%. In healthy subjects, the mean (± SD) plasma half-life was 1.5 (± 1.0) hours. Both $C_{max}$ and AUC are diminished by about 50% if the drug is given 30 minutes after food as opposed to the fasting condition. There if no significant food effect if the drug is given before meals.

**Distribution**

Lansoprazole is 97% bound to plasma proteins. Plasma protein binding is constant over the concentration range of 0.05 to 5.0 μg/mL.

**Metabolism**

Lansoprazole is extensively metabolized in the liver. Two metabolites have been identified in measurable quantities in plasma (the hydroxylated sulfinyl and sulfone derivatives of Lansoprazole). These metabolites have very little or no antisecretory activity.

Lansoprazole is thought to be transformed into two active species which inhibit and secretion by $(H^+K^+)$-ATPase within the parietal cell canaliculus, but are not present in the systemic circulation. The plasma elimination half-life of Lansoprazole does not reflect its duration of suppression of gastric acid secretion. Thus, the plasma elimination half-life is less than two hours, while the acid inhibitory effect lasts more than 24 hours.

**Elimination**

Following single-dose oral administration of Lansoprazole, virtually no unchanged Lansoprazole was excreted in the urine. This implies a significant billiary excretion of the metabolites of Lansoprazole.

## 5.3 Pre Clinical Safety Data

### Carcinogenicity, Teratogenicity and Impairment of fertility

In two 24-month Carcinogenicity studies, Sprague - Dawley Rats were treated orally with doses of 5 to 250 mg / day, about 1 to 40 times the exposure on a body surface ($mg/m^2$) basis of a 50 - kg person of average height (1.46 $m^2$ body surface area) given the recommended human dose of 30 mg / day (22.2 mg/ $mg^2$). Lansoprazole produced dose-related gastric enterochromaffin - like (ECL) cell hyperplasia and ECL cell carcenoids in both male and female rats. It also increased the incidence of intestinal metaplasia of the gastric epithelium in both sexes. In male rats, Lansoprazole produced a dose-related increase of testicular interstitial cell adenomas. The incidence of these adenomas in rats receiving doses of 15 to 150 mg / kg / day (4 to 40 times the recommended human dose based on body surface area) exceeded the low background incidence (range = 1.4 to 10%) for this strain of rat. Testicular interstitial cell adenoma also occurred in 1 of 30 rats treated with 50 mg / kg /day (13 times the recommended human dose based on body surface area) in a 1-year toxicity study.

In a 24 month carcinogenicity study, CD-1 mice were treated orally with doses of 15 to 600 mg/kg/day, 2 to 80 times the recommended human dose based on body surface area. Lansoprazole produced a dose-related increased incidence of liver tumors (hepatocellular adenoma plus carcinoma). The tumor incidences in male mice treated with 300 and 600 mg / kg / day (40 to 80 times the recommended human dose based on body surface area) and female mice treated with 150 to 600 mg / kg/ day (20 to 80 times the recommended human dose based on body surface area) exceeded the ranges of background incidences in historical controls for this strain of mice. Lansoprazole treatment produced adenoma of rat testis in male mice receiving 75 to 600 mg / kg / day (10 to 30 times the recommended human dose based on body surface area).

Lansoprazole was not genotoxic in the Ames test, the ex- vivo rat hepatocyte unscheduled DNA synthesis (UDS test, the in-vivo mouse micronucleus test or the bone marrow cell chromosomal aberration assays.
Lansoprazole at oral doses up to 150 mg / kg /day (40 times the recommended human dose based on body surface area) was found to have no effect on fertility and reproductive performance of male and female rats.

### Teratogenic Effects

Teratology studies have been performed in pregnant rats at oral doses of up to 150 mg / kg / day (40 times the recommended human dose based on body surface area) and pregnant rabbits at oral doses of up to 40 mg / kg / day (16 times the recommended human dose based on body surface area) and have revealed no evidence of impaired fertility or harm to the fetus due to Lansoprazole. There are, however, no adequate or well controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

## 6. Pharmaceutical Particulars

### 6.1 List of Excipients

Not Applicable

### 6.2 Incompatibilities

None Reported

### 6.3 Shelf life

24 months from the date of manufacturing.

### 6.4 Special Precautions for Storage

Store at a temperature not exceeding 25°C, protect from light and moisture.

### 6.5 Nature and Content of Container

Zapacid 30 Capsules are packed in Printed Aluminium foil and clear PVC rigid film coated with PVdC.

Box of 3x10's

### 6.6 Instructions for use/handling

Not Applicable

## 7. Marketing Authorization Holder

Win-Medicare Pvt. Ltd.
1400, Modi Tower
98, Nehru Place
New Delhi – 110019, India.

## 8. Marketing Authorization Number

Registration Number: B4-2382

## 9. Date of first Authorization/Renewal of the Authorization

6th May 2014

## 10. Date of Revision of the Text

October, 2019

### 1.3.2 Labelling (outer & inner labels)

Please find the enclosed mock ups of Zapacid Capsules 30 mg.