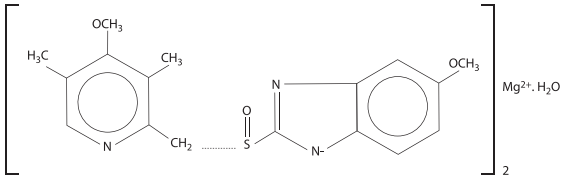
Esorest

20mg & 40mg

(Esomeprazole)

ESOREST is supplied as delayed-release capsules for oral administration. Each delayed-release capsule contains 20 mg or 40 mg of esomeprazole as esomeprazole magnesium in the form of enteric-coated pellets. Esomeprazole is the S-isomer of omeprazole, which inhibits gastric acid secretion more effectively than omeprazole.

Esomeprazole is used to treat certain conditions caused by too much acid being produced in the stomach, such as stomach ulcers (gastric ulcers), ulcers ofthe upper part ofthe intestine (duodenal ulcers), and reflux oesophagitis (acid reflux or heartburn).
Chemically it is bis (5-methoxy-2-[(S)-[(4-methoxy-3,5-dimethy l-2-pyridinyl) methyl]sulfinyl) -1H-benzimidazole-1-yl) magnesium trihydrate. Its empirical formula is (C"H"N,O,S),Mg.3H,O



COMPOSITION
ESOREST capsule 20 mg
Each capsule contains:
Enteric coated pellets of esomeprazole magnesium trihydrate
equivalent to esomeprazole... ... ... 20 mg.

ESOREST capsule 40 mg
Each capsule contains:
Enteric coated pellets of esomeprazole magnesium trihydrate
equivalent to esomeprazole... ... ... 40 mg.

CLINICAL PHARMACOLOGY
Mechanism of Action
Esomeprazole is a proton pump inhibitor that suppresses gastric acid secretion by specific inhibition of the H^+/ K^+-ATPase in the gastric parietal cells. By acting specifically on the proton pump, esomeprazole blocks the final step in acid production, thus reducing gastric acidity.

Pharmacokinetics

Absorption
After oral administration peak plasma concentration (Cmax) occurs at approximately 1.5 hours. The peak plasma concentration increases proportionally with increase in dose from 20 mg to 40 mg. The systemic bioavailability of esomeprazole increases with both dose and repeated administration to about 68% to 89% for doses of 20 and 40 mg respectively.

Effects of food: Food delays and decreases the absorption of esomeprazole, but this does not significantly change its effect on intragastric acidity. After oral administration of a single 40 mg dose, theAUC is decreased by 43% to 53% after food intake compared to fasting condition. Esomeprazole should be taken at least one hour before meals.

Distribution
Esomeprazole is about 97% bound to plasma proteins. The apparent volume of distribution at steady state in healthy volunteers is about 16 L.

Metabolism
Esomeprazole is extensively metabolized in the liver by the cytochrome P450 isoenzyme CYP2C19 to hydroxy and desmethyl metabolites, which have no effect on gastric acid secretion. The remainder is metabolized by the cytochrome P450 isoenzyme CYP3A4 to esomeprazole sulfone. With repeated administration, there is a decrease in first-pass metabolism and systemic clearance, probably caused by an inhibition of the CYP2C19 isoenzyme. However there is no accumulation during once daily administration.

Excretion
The plasma elimination half-life is about 1.3 hours. Almost 80% of an oral dose is eliminated as metabolites in the urine, the remainder in the feces.

Special populations

Geriatric
The elimination rate of esomeprazole is somewhat decreased in the elderly, and bioavailability is slightly increased. Dosage adjustment based on age is not necessary.

Pediatric
Pharmacokinetic data in the pediatric population(18 yrs of age) are not available.

Gender
The values of AUC and Cmax are slightly higher in females than in males at steady state. Dose adjustment based on gender is not necessary.

Renal Insufficiency
As only less than 1% of esomeprazole is excreted unchanged in urine, the pharmacokinetics of esomeprazole in patients with renal impairment are not expected to be changed relative to healthy volunteers.

Hepatic Insufficiency
No dose adjustment is recommended for patients with mild to moderate hepatic insufficiency. However, in patients with severe hepatic insufficiency, a dose of 20 mg once daily should not be exceeded.

INDICATIONS:
ESOREST is indicated for:

1. Gastroesophageal Reflux Disease (GERD)
- The treatment of erosive esophagitis

- Long term management of patients with healed esophagitis to prevent relapse.
- Symptomatic treatment of gastroesophageal reflux disease (GERD) without esophagitis.

2. Triple therapy for the eradication of Helicobacter pylori
Esomeprazole is combined with the antbiotics clarithromycin and amoxicillin (or metronidazole in penicillin-hypersensitive patients) for the eradication of *Helicobacter pylori*. Infection by *H. pylori* is the causative factor in the majority of peptic and duodenal ulcers.

Note: In patients who failed the therapy. susceptibility testing should be done. If resistance to clarithromycin is demonstrated or susceptibility testing is not possible, alternative antimicrobial therapy should be instituted.

DOSAGE AND ADMINISTRATION:
ESOREST capsules should be taken at least one hour before meals.

1. Gastroesophageal Reflux Disease
- Healing of erosive esophagitis
40 mg or 20 mg once daily for 4 to 8 weeks (an additional 4 to 8 week treatment may be considered if symptoms persist or esophagitis does not heal).

- *Maintenance of healing erosive esophagitis*
20 mg once daily.

- *Symptomatic gastroesophageal reflux disease without esophagitis*
20 mg or 40 mg once daily for 4 weeks (an additional 4 to 8 week treatment may be considered if symptoms do not resolve completely).

2. H.pylori eradication to reduce the risk of duodenal ulcer recurrence
ESOREST : 40 mg once daily for 10 days.
Amoxicillin: 1000 mg twice daily for 10 days.
Clarithromycin: 500 mg twice daily for 10 days.

For patients with severe liver impairment (Child Pugh Class C), a dose of 20 mg of ESOREST (Esomeprazole) should not be exceeded.

ADVERSE REACTIONS
Esomeprazole, like other PPIs **(Proton Pump Inhibitor)**, is well-tolerated. The most common side effects are diarrhoea, nausea, vomiting, constipation, flatulence,headache, hypertension, tachycardia, skin rashes, itching, dizziness, swollen extremities (fingers and toes etc.), muscle and joint pain, cramps, general feeling of being unwell, blurred vision, depression and dry mouth.

CONTRAINDICATIONS
ESOREST (Esomeprazole) is contraindicated in patients with known hypersensitivity to any component of the formulation or to substituted benzimidazoles.

Drug Interactions
As esomeprazole inhibits gastric acid secretion, it may interfere with the absorption of drugs for which gastric pH is important for bioavailability e.g. ketoconazole, iron salts, atazanavir & digoxin.

Esomeprazole inhibits CYP2C19, the major esomeprazole metabolizing enzyme. Thus, when esomeprazole is combined with drugs metabolized by CYP2C19, such as diazepam, citalopram, imipramine, clomipramine, phenytoin etc., the plasma concentrations of these drugs may be increased and a dose reduction could be needed.

PRECAUTIONS
General
In the presence of any alarming symptoms (e.g. significant unintentional weight loss, recurrent vomiting, dysphagia, haematemesis or melaena) and when gastric ulcer is suspected or present, malignancy should be excluded, as treatment with esomeprazole may alleviate symptoms and delay diagnosis.

Atrophic gastritis has been noted occasionally in gastric corpus biopsies from patients treated long-term with omeprazole, of which esomeprazole is an enantiomer.

When prescribing esomeprazole for eradication of Helicobacter pylori infection possible drug interactions for other components in the triple therapy should be considered.

Pediatric Use
Safety and effectiveness in pediatric patients have not been established.

Pregnancy
There are no adequate and well-controlled studies in pregnant women. Esomeprazole should be used during pregnancy only if clearly needed.

Nursing Mothers
Because esomeprazole is likely to be excreted in human milk, because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account importance of the drug to the mother.

STORAGE:
Store between 15-30°C in a dry place,
protect from light.
To be dispensed on the prescription of a
registered medical practitioner only.
Keep out of the reach of children.

AVAILABILITY:
ESOREST 20 mg and 40 mg are available in Alu-Alu blister pack of 2 x 7 capsules.

Manufactured by:
Kaizen Pharmaceuticals (Pvt.) Ltd.
E-127-129, North Western industrial Zone,
Bin Qasim, Karachi-75020, Pakistan.

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