Espra®
(Esomeprazole)
20mg, 40mg Capsules

DESCRIPTION
Espra 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 of the upper part of the intestine (duodenal ulcers), and reflux esophagitis (acid reflux or heartburn). Chemically, it is bis[(S)-methyl-2,3-dimethyl-2-pyrindinylmethylsulfanyl]-1H-benzimidazol-1-yl)magnesium trihydrate. Its empirical formula is (C₁₇H₂₈N₄O₄S)·Mg·3H₂O.

COMPOSITION:
Esomeprazole 20mg
Each capsule contains:
Esomeprazole Magnesium (Manufacturer’s Specs.) equivalent to
Esomeprazole .................................................. 20 mg.
(CCL Pharmaceuticals Specifications)

Esomeprazole 40mg
Each capsule contains:
Esomeprazole Magnesium (Manufacturer’s Specs.) equivalent to
Esomeprazole .................................................. 40 mg.
(CCL Pharmaceuticals Specifications)

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 to 40mg. The systemic bioavailability of esomeprazole increases with both dose and repeated administration to about 68% to 89% for doses of 20 and 40mg 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 40mg dose, the AUC is decreased by 42 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 16L.

Metabolism
Esomeprazole is extensively metabolized in the liver by the cytochrome P450 isozyme CYP2C19 to hydroxy and desmethyl metabolites, which have no effect on gastric acid secretion. The remainder is metabolized by the cytochrome P450 isozyme 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 isozyme. 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 faeces.

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 years 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 20mg once daily should not be exceeded.

INDICATIONS:
1. Gastroesophageal Reflux Disease (GERD)
Espra is indicated for:
- 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 antibiotics 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.

DOSE AND ADMINISTRATION:
Espra capsules should be taken at least one hour before meals.

1. Gastroesophageal Reflux Disease
- Healing of erosive esophagitis
40mg or 20mg 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
20mg once daily.
- Symptomatic gastroesophageal reflux disease without esophagitis
20mg or 40mg 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
Espra: 40mg once daily for 10 days.
- Clarithromycin: 500mg twice daily for 10 days.
- Amoxicillin: 1000mg twice daily for 10 days.
- For patients with severe liver impairment (Child Pugh Class C), a dose of 20mg of Espra (Esomeprazole) should not be exceeded.

ADVERSE REACTIONS
Esomeprazole, like other PPIs, is well-tolerated. The most common side effects are diarrhea, 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
Espra (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 and digoxin.

Esomeprazole inhibits CYP2C19, the major esomeprazole metabolizing enzyme. Thus, when esomeprazole is combined with drugs metabolized by CYP2C19, such as diazepam, cilostapram, 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 melena) 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.

Espra capsule should be taken at least one hour before meals.

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.

INSTRUCTIONS:
- Store below 30°C.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- To be sold on the prescription of a registered medical practitioner only.

AVAILABILITY:
Espra 20mg and 40mg are available in Alu tropical covering blister pack of 2 x 7 capsules.

For further information please contact.