ORTESO

(Esomeprazole)

Capsules

COMPOSITION:

Each delayed release 40mg capsule contains:
Esomeprazole Magnesium trihydrate Pellets eq. to Esomeprazole..... 40mg (Orta specs.)

DESCRIPTION

Orteso is supplied as delayed. release Capsules for oral administration. Orteso capsules are an enteric coated pellet formulation of Esomeprazole Magnsium due to its acid labile nature. Esomeprazole is the S-isomer of Omeprazole, which inhibits gastric acid secretion more effectively than Omeprazole.

CLINICAL PHARMACOLOGY:

Pharmacodynamics

Mechanism of Action

Esomeprazole is a proton pump inhibitor that suppress gastric acid secretion by specific inhibition of the H+/K+-ATPase in the gastric parietal cell. The S- and R-isomors of Omeprazole are protonat. and converted in the acidic cornpartment of the parietal .11 forming the active inhibitor, the achiral sulphenamide. By acting specifically on theOroton pump, esomeprazole blocks the fi.l step in acid production, thus reducing gastric acidity. This effect is dose-related up to a daily do. of 40mg and leads to inhibition of gastric acid secretion.

Pharmacokinetics:

Esomperazole is rapidly absorbed after oral administration, with peak plasma levels occuring after approximately 1 to 2 hours. It is acid labile and an enteric-coated formulation has been developed. Food delays and decreases the absorption of esomeprazole, but this does not significantly change its effect on intragastric acidity. Esomeprazole is about 97%, bound to plasma proteins. It is extensively metabolised in the liver by the cytochrome P450 isoenzyme CYP2CIP to hydroxy, and desmethyl metabolits, which have no effect on gastric acidsecretion. The remainder is metabolised by the cytochrome P450 isoenzyme CYP3A4 to esomeprazole sulfone. With repeate 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. The plasma elimination half-life is about 1.3hours. Almost 80% of an oral dose, is eliminated as metabolites in the urine, the remainder in the feces.

Excretion:

Tagtoatiplasma clearance is 17L/h after a single dose and about 9L/H after repeated administration. The plasma elimination half-life of esomeprazole is approximately. 1-1.5 hours. Less then1% of the parent during is excreted in the urie, Approximately 80% of an oral dose of esomeprazole is excreted as inactive metabolites in the urine, and the remainder is found an in active metabolites in thefeces.

Special Populations:

Geriatric

The AUC and Cmax values were slightly higher (25% and 18% respectively) in the elderly as compared to younger subjects at steady state. Dose adjustment based on age is not necessary.

Hepatic Insufficiency:

In patientws witgh mild and moderate hepatic insufficiency, the AUCs were in the range that could be expected in the patients with normal liver function. In patients with severe hepatic insufficiency the AUCs were 2 to 3 times higher than in the patients with normal liver function. No dose adjustment is recommended for patients with mild to moderate hepatic insufficiency (child pugh classes A and B)

Renal Insufficiency:

The pharmacokinetics of esomeprazole in patients with renal impairment are not expected to be altered relative to healthy volunteers, as less than 1% of esomeprazole is excreted unchanged in urine.

THERAPEUTIC INDICATIONS:

Orteso (Esomeprazole) is indicated for:

1. Gastroesophageal Reflux Disease (GERD)
   - Treatment of erosive reflux esophagitis
   - Long term management of patients with healed esophagitis to prevent relaose.
   - Symptomatic treatment of gastroesophageal reflux disease (GERD) without esophagitis.
2. As a triple therapy (Esomeprazole plus amoxicillin and clarithromycin) for the eradication of helicobacter pylori.
   - Healing of duodenal ulcer associated with heling of duidenal ulcer associated with helicobacter pylori infection.
   - Prevention of relapse of peptic ulcers in patients with helicobacter pylori, associated ulcers.

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

Dosage and administration:

The usual dose for the treatment of gastro-esophageal reflux disease is 40mg by mouth once daily for 4 weeks.

Children

In children.doses in the range 0.7 to 1.4 mg per kg body weight daily, up to maximum daily dose of 40mg, have been given for 4 to 12 weeks.

The recommended adult dosages are outlined in the table below. Orteso capsules should be swallowed whole and taken at least one hour before meals.

Recommended Adult Dosage Schedule

Indication	Dosage	Frequency
1. Gastroesophageal Reflux Disease Healing of erosive esophagits	40mg	One daily for 4 to 8 Weeks (an additional 4-8 weeks Treatment may be donsidered if symptoms persist to esophagits does not heal)
Symptomatic gastroesophageal refulx disease without esophagitis	40mg	One daily for 4 to 8 Weeks (an additional 4-8 weeks treatment may be donsidered if symptoms do not resolve completely)
II. H. Pylori eradication to reduce the risk of duodenal ulcer recurrence Orteso Amoxicillin Clarithromycin	 40mg 1000mg 500mg	 One daily for 10 days Twice daily for 10 days Twice daily for 10 days

CONTRA-INDICATIONS:

Orteso (Esomeprazole) is contraindicated inpatients with known hypersensitivity to drug or any component of the formulation or to substitiuted benzimidazoles.

ADVERSE EFFECTS:

Following are some common, uncommon and rare adverse drug reactions have been reported during the treatment of esomeprazole.

Common:

- *Headache
- *Abdominal pain
- *Diarhoea
- *Flatulence
- *Nausea/Vomiting
- *Constipation

Uncommon:

- *Dermatitis
- *Prutitus
- *Urticaria
- *Dizziness
- *Dry Mouth

Rare: Hypersensitivity reactions e.g angloedema, anaphylactic reactions

PRECAUTIONS:

Before giving esomeprazole or other proton pump Inhibitor to patients with gastric ulcers the possibility of malignancy should be considered since these drugs may mask symptoms and delay diagnosis Esomeprazole and other proton pump inhibitors Should be used with caution in hepatic impairment.

- When prescribing esomeprazole for an on-demand therapy, the implication for intractions with other pharmaceuticals, due to fluctuating plasma concentrations of esomeprazole should be conisdered.
- When prescribing esomeprazole for eradication of helicobacter pylori infecton possible drug interactions for other components in the triple therapy should be considered.
- Patients with rare herediatary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

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 excreated in human milk a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account importance of the drug to the mother due to the potential for adverse reactions in nursing infants from esomeprazole.

Storage:

Store at 15-30°C in a dry and dark place.

Presentation:

Orteso Capsules 40mg.....(2x7's) blister

ORTA SINCE 1954

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ORTA LABORATORIES (PVT.) LTD.
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