Sergel®

Esomeprazole USP

Active ingredient

Sergel® 20mg capsules: Each capsule contains Esomeprazole Magnesium Trihydrate USP 22.27 mg equivalent to 20 mg Esomeprazole in enteric coated pellets.

Sergel® 40mg capsules: Each capsule contains Esomeprazole Magnesium Trihydrate USP 44.54 mg equivalent to 40 mg Esomeprazole in enteric coated pellets.

Sergel® 20mg tablets: Each enteric coated tablet contains Esomeprazole Magnesium Trihydrate USP 22.27 mg equivalent to 20 mg Esomeprazole.

Sergel® 40mg tablets: Each enteric coated tablet contains Esomeprazole Magnesium Trihydrate USP 44.54 mg equivalent to 40 mg Esomeprazole.

Sergel® 20 mg sachets: Each sachet contains Esomeprazole Magnesium Trihydrate USP 22.27 mg equivalent to 20 mg of Esomeprazole as enteric-coated microgranules.

Properties and effects

Esomeprazole is a proton pump inhibitor that suppresses gastric acid secretion by specific inhibition of the H^+/K^+-ATPase, the 'Proton Pump' of the gastric parietal cell.

Indication

Esomeprazole is indicated

- To relieve from chronic heartburn symptoms and other symptoms associated with GERD
- For the healing of erosive esophagitis
- For maintenance of healing of erosive esophagitis
- In combination with amoxicillin and clarithromycin for eradication of *Helicobacter pylori* infection in-patients with duodenal ulcer disease.
- Zollinger-Ellison Syndrome
- Acid related Dyspepsia
- Duodenal & Gastric ulcer

Pharmacokinetics

Absorption

Esomeprazole capsules contain an enteric-coated pellet formulation of esomeprazole magnesium. After oral administration peak plasma levels (C_{max}) occur at approximately 1.5 hours (T_{max}). The C_{max} increases proportionally when the dose is increased, and there is a three-fold increase in the area under the plasma concentration- time curve (AUC) from 20 to 40 mg. At repeated once daily dosing, the systemic bioavailability is approximately 90% compared to 64% after a single dose. The AUC after administration of a single dose of esomeprazole is decreased by 33-53% after food intake compared to fasting conditions. Esomeprazole should be taken at least one hour before meals.

Distribution

Esomeprazole is 97% bound to plasma proteins. Plasma protein binding is constant over the concentration range of 2-20 mol/L. The apparent volume of distribution at steady state in healthy volunteers is approximately 16 L.

Metabolism

Esomeprazole is extensively metabolised in the liver by the cytochrome P450 (CYP) enzyme system. The metabolites of esomeprazole lack antisecretory activity. The major part of esomeprazole's metabolism is dependent upon the CYP2C19 isoenzyme, which forms the hydroxy and desmethyl metabolites. The remaining amount is dependent on CYP3A4 which forms the sulphone metabolite.

Excretion

The plasma elimination half-life of Esomeprazole is approximately 1–1.5 hours. Less than 1% of parent drug is excreted in the urine. Approximately 80% of an oral dose of esomeprazole is excreted as inactive metabolites in the urine, and the remainder is found as inactive metabolites in the faeces.

Combination Therapy with Antimicrobials

Esomeprazole Magnesium 40 mg once daily is given in combination with clarithromycin 500 mg twice daily and amoxicillin 1000 mg twice daily for 7 days. The mean steady state AUC and C_{max} of Esomeprazole increased by 70% and 18%, respectively, during triple combination therapy compared to treatment with Esomeprazole alone.

The pharmacokinetic parameters for clarithromycin and amoxicillin are similar during triple combination therapy and administration of each drug alone. However, the mean AUC and C_{max} for 14-hydroxyclarithromycin are increased by 19% and 22%, respectively, during triple combination therapy compared to treatment with clarithromycin alone. This increase in exposure to 14-hydroxyclarithromycin is not considered to be clinically significant.

Dosage & Administration

Esomeprazole should be swallowed whole and taken one hour before meal.

Healing of Erosive Esophagitis: 20 mg or 40 mg Once Daily for 4-8 Weeks. The majority of patients are healed within 4 to 8 weeks. For patients who don't heal after 4-8 weeks, an additional 4-8 weeks of treatment may be considered. *Maintenance of Healing of Erosive Esophagitis:* 20 mg Once Daily *(Clinical studies did not extend 6 months)*. Symptomatic GERD: 20 mg Once Daily for 4 Weeks. If symptoms do not resolve completely after 4 weeks, an additional 4 weeks of treatment may be considered. *Helicobacter Pylori eradication:* Triple Therapy to reduce the risk of Duodenal Ulcer recurrence-Esomeprazole 40 mg Once Daily for 10 days, Amoxicillin 1000 mg Twice Daily for 10 days, Clarithromycin 500 mg Twice Daily for 10 days. *Zollinger-Ellison Syndrome:* The dose is 20-80 mg once daily. The dosage should be adjusted individually and treatment continued as long as clinically indicated. *Acid related Dyspepsia:* 20-40 mg once daily for 2-4 weeks according to response. *Duodenal ulcer:* 20 mg once daily for 2-4 weeks. *Gastric ulcer:* 20-40 mg once daily for 4-8 weeks.

Direction for use of Delayed-Release Oral Suspension

Whole contents of the packet should be taken into a small glass containing 15 ml. of water. The mixer should be stirred well and leave 2 to 3 minutes to thicken. Stir again and drink within 30 minutes. If any medicine remains after drinking, add more water, stir, and drink immediately.

If the suspension is to be administered through a nasogastric or gastric tube, the volume of water in the syringe should be 15 ml. & immediately shake the syringe and leave 2 to 3 minutes to thicken. Shake the syringe and inject through the nasogastric or gastric tube into stomach within 30 minutes. An appropriately sized syringe should be used. Shake and flush any remaining contents from nasogastric or gastric tube into the stomach.

Contraindication

Esomeprazole is contraindicated in-patient with known hypersensitivity to any of the formulation.

Precaution

General

Symptomatic response to therapy with esomeprazole does not preclude the presence of gastric malignancy.

Information for patients

Esomeprazole capsules should be taken at least one hour before meals. For patients who have difficulty swallowing capsules, one tablespoon of applesauce can be added to an empty bowl and the Esomeprazole capsules can be opened, and the pellets inside the capsule carefully emptied onto the applesauce. The pellets should be mixed with the applesauce and then swallowed immediately. The applesauce used should not be hot and should be soft enough to be swallowed without chewing. The pellets should not be chewed or crushed. The pellet/applesauce mixture should not be stored for future use. Antacids may be used while taking esomeprazole.

Pregnancy

There are no adequate and well-controlled studies in pregnant women. Animal studies have revealed no teratogenic effects.

Nursing Mothers

The excretion of esomeprazole in milk has not been studied. Breast-feeding should be therefore be discontinued if the use of esomeprazole is considered essential.

Paediatric Use

Safety and effectiveness in paediatric patients have not been established.

Geriatric Use

No overall differences in safety and efficacy have been observed between the elderly and younger individuals, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

Hepatic Insufficiency

No dosage 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.

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.

Undesirable effects

The most frequently occurring adverse events reported with Esomeprazole include headache, diarrhoea, nausea, flatulence, abdominal pain, constipation and dry mouth. There are no difference in types of related adverse events seen during maintenance treatment upto 12 months compared to short term treatment.

Drug Interaction

Esomeprazole is extensively metabolized in the liver by CYP2C19 and CYP3A4. In vitro and in vivo studies have shown that Esomeprazole is not likely to inhibit CYPs 1A2, 2A6, 2C9, 2D6, 2E1 and 3A4. No clinically relevant interactions with drugs metabolized by these CYP enzymes would be expected. Drug interaction studies have shown that Esomeprazole does not have any clinically significant interactions with phenytoin, warfarin, quinidine, clarithromycin or amoxicillin.

Esomeprazole may potentially interfere with CYP2C19, the major Esomeprazole metabolising enzyme. Co-administration of Esomeprazole 30 mg and diazepam, a CYP2C19 substrate has resulted in a 45% decrease in clearance of diazepam. Increased plasma levels of diazepam have been observed 12 hours after dosing and onwards. Esomeprazole inhibits gastric acid secretion. Therefore, Esomeprazole may interfere with the absorption of drugs where gastric pH is an important determinant of bioavailability (e.g., ketoconazole, iron salts and digoxin).

Co-administration of oral contraceptives, diazepam, phenytoin, or quinidine do not seem to change the pharmacokinetic profile of Esomeprazole.

Combination Therapy with Clarithromycin

Co-administration of esomeprazole, clarithromycin, and amoxicillin has resulted in increases in the plasma levels of esomeprazole and 14-hydroxyclarithromycin.

Overdose

A single oral dose of Esomeprazole at 510 mg/kg (about 103 times the human dose on a body surface area basis), has been lethal to rats. The major signs of acute toxicity are reduced motor activity, changes in respiratory frequency, tremor, ataxia, and intermittent clonic convulsions. There have been no reports of overdose with Esomeprazole.

No specific antidote for Esomeprazole is known. Since Esomeprazole is extensively protein bound, it is not expected to be removed by dialysis. In the event of overdosage, treatment should be symptomatic and supportive. As with the management of any overdose, the possibility of multiple drug ingestion should be considered.

Packs

Sergel® 20mg capsules: Each box contains 10x10's capsules in Alu-Alu blister pack.

Sergel® 40mg capsules: Each box contains 5x10's capsules in Alu-Alu blister pack.

Sergel® 20mg tablets: Each box contains 3x10's tablets in Alu-Alu blister pack.

Sergel® 40mg tablets: Each box contains 3x10's tablets in Alu-Alu blister pack.

Sergel® 20mg sachets: Each box contains 30 sachets.

Storage

Store at temperature not exceeding 30 °C in a dry place. Protect from light and moisture.

Medicine: Keep out of reach of children.

Healthcare

Manufactured by

Healthcare Pharmaceuticals Ltd.

Rajendrapur, Gazipur, Bangladesh

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