SOMEZOL® Capsules

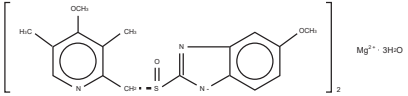
(E s o m e p r a z o l e)

سومیزول کیپسولز

(ایسومیپرازول)

DESCRIPTION :

The active ingredient in SOMEZOL (Esomeprazole) is bis(5-methoxy-2-[(S)-[(4-methoxy-3,5- dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole-1-yl) magnesium trihydrate, a compound that inhibits gastric acid secretion more effectively than omeprazole. Esomeprazole is the S-isomer of omeprazole, which is a mixture of the S- and R- isomers. Its empirical formula is $(C_{17}H_{18}N_3O_3S)_2$ Mg x 3 H_2O with molecular weight of 767.2 as a trihydrate and 713.1 on an anhydrous basis. The structural formula is:



The magnesium salt is a white to slightly colored crystalline powder. It contains 3 moles of water of solvation and is slightly soluble in water.

COMPOSITION :

SOMEZOL Capsules 20mg :

Each capsule contains:

Esomeprazole ..... 20mg as Esomeprazole Magnesium Trihydrate U.S.P. (Enteric Coated Pellets)

(Product Specs.: U.S.P.)

SOMEZOL Capsules 40mg :

Each capsule contains:

Esomeprazole ..... 40mg as Esomeprazole Magnesium Trihydrate U.S.P. (Enteric Coated Pellets)

(Product Specs.: U.S.P.)

CLINICAL PHARMACOLOGY :

Pharmacokinetics

Absorption

SOMEZOL Capsules contain an enteric-coated pellet formulation of Esomeprazole magnesium. After oral administration peak plasma levels (Cmax) occur at approximately 1.5 hours (Tmax). The Cmax 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 with 40 mg, the systemic bioavailability is approximately 90% compared to 64% after a single dose of 40mg.

Effect of food: The AUC after administration of a single 40 mg dose of Esomeprazole is decreased by 43-53% after food intake compared to fasting conditions. Esomeprazole should be taken at least one hour before meals. Food delays and decreases the absorption of Esomeprazole, but this does not significantly change its effect on the intra gastric acidity.

Distribution

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

Metabolism
Esomeprazole is extensively metabolized 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 feces.
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. Dosage adjustment based on age is not necessary.
Pediatric
The pharmacokinetics of Esomeprazole have not been studied in patients < 18 years of age.
Gender
The AUC and Cmax values were slightly higher (13%) in females than in males at steady state. Dosage adjustment based on gender is not necessary.
Hepatic Insufficiency :
In patients with mild and moderate hepatic insufficiency, the AUCs were within the range that could be expected in 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 dosage adjustment is recommended for patients with mild to moderate hepatic insufficiency (Child Pugh Classes A and B). However, in patients with severe hepatic insufficiency (Child Pugh Class C) 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.
Pharmacodynamics :
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 cell. The S- and R-isomers of omeprazole are protonated and converted in the acidic compartment of the parietal cell forming the active inhibitor, the achiral sulphenamide. By acting specifically on the proton pump, Esomeprazole blocks the final step in acid production, thus reducing gastric acidity. This effect is dose-related up to a daily dose of 20 to 40 mg and leads to inhibition of gastric acid secretion.
Microbiology :
Esomeprazole magnesium, amoxicillin and clarithromycin triple therapy has been shown to be active against most strains of Helicobacter pylori (H. pylori) in vitro and in clinical infections.

INDICATIONS AND USAGE :
Treatment of Gastroesophageal Reflux Disease (GERD)
Healing of Erosive Esophagitis
SOMEZOL is indicated for the short-term treatment (4 to 8 weeks) in the healing and symptomatic resolution of diagnostically confirmed erosive esophagitis. For those patients who have not healed after 4-8 weeks of treatment, an additional 4-8-week course of SOMEZOL may be considered.
Maintenance of Healing of Erosive Esophagitis
SOMEZOL is indicated to maintain symptom resolution and healing of erosive esophagitis.
Symptomatic Gastroesophageal Reflux Disease
SOMEZOL is indicated for treatment of heartburn and other symptoms associated with GERD.
Risk Reduction of NSAID-Associated Gastric Ulcer
SOMEZOL is indicated for the reduction in the occurrence of gastric ulcers associated with continuous NSAID therapy in patients at risk for developing gastric ulcers. Patients are considered to be at risk due to their age (> 60) and/or documented history of gastric ulcers.

H. pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence
Triple Therapy (SOMEZOL plus amoxicillin and clarithromycin): SOMEZOL, in combination with amoxicillin and clarithromycin, is indicated for the treatment of patients with H. pylori infection and duodenal ulcer disease (active or history of within the past 5 years) to eradicate H. pylori.
Eradication of H. pylori has been shown to reduce the risk of duodenal ulcer recurrence. In patients who fail 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 :
The recommended adult dosages are outlined in the table below. SOMEZOL Capsules should be swallowed whole and taken at least one hour before eating.

Recommended Adult Dosage Schedule		
Indication	**Dose**	**Frequency**
I. Gastroesophageal Reflux Disease		
Healing of erosive esophagitis	20mg or 40mg	Once daily 4 to 8 weeks (an additional 4-8 weeks 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 4-8 weeks treatment may be considered if symptoms does not resolve completely)
II. H. Pylori eradication to reduce the risk of duodenal ulcer recurrence		
Somezol Amoxicillin Clarithromycin	40mg 1g 500mg	Once daily for 10 days Twice daily for 10 days Twice daily for 10 days

Special Populations : Geriatric
No dosage adjustment is necessary.
Renal Insufficiency
No dosage adjustment is necessary.
Hepatic Insufficiency
No dosage adjustment is necessary in patients with mild to moderate liver impairment (Child Pugh Classes A and B). For patients with severe liver impairment (Child Pugh Class C), a dose of 20 mg of SOMEZOL should not be exceeded.
Gender : No dosage adjustment is necessary

CONTRAINDICATIONS :
SOMEZOL is contraindicated in patients with known hypersensitivity to any component of the formulation or to substituted benzimidazoles.

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. Patients on long term treatment (particularly those treated for more than a year) should be kept under regular surveillance since the symptomatic response to therapy with Esomeprazole does not preclude the gastric malignancy.

Drug Interactions
Drug interaction studies have shown that Esomeprazole does not have any clinically significant interactions with phenytoin, warfarin, quinidine, clarithromycin or amoxicillin. Coadministration of oral contraceptives, diazepam, phenytoin, or quinidine did not seem to change the pharmacokinetic profile of Esomeprazole. Esomeprazole inhibits gastric acid secretion. Therefore, Esomeprazole may interfere with the absorption of drugs where gastric pH is an important determinant of bioavailability (eg. ketoconazole, iron salts and digoxin).

Pregnancy
Teratogenic Effects : Pregnancy Category B - Teratology studies have been performed in rats at oral doses up to 280 mg/kg/day (about 57 times the human dose on a body surface area basis) and in rabbits at oral doses up to 86 mg/kg/day (about 35 times the human dose on a body surface area basis) and have revealed no evidence of impaired fertility or harm to the fetus due to Esomeprazole. There are, however, no adequate and 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.

Nursing Mothers
The excretion of Esomeprazole in milk has not been studied. However, omeprazole concentrations have been measured in breast milk of a woman following oral administration of 20 mg. Because Esomeprazole is likely to be excreted in human milk, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

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

Geriatric Use
No overall differences in safety and efficacy were 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.

ADVERSE REACTIONS :
The following adverse drug reactions have been reported during therapy of Esomeprazole. None found to be dose-related
Common: Headache, abdominal pain, diarrhoea, flatulence, nausea/vomiting, constipation
Uncommon: Dermatitis, pruritis, urticaria, dizziness, dry mouth
Rare: Hypersensitivity reactions e.g. angioderma, anaphylactic reaction

OVERDOSAGE :
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 over dosage, treatment should be symptomatic and supportive.
As with the management of any overdose, the possibility of multiple drug ingestion should be considered.

Shelf Life: 03 Years

HOW SUPPLIED :
SOMEZOL 20mg : Cold Form & Cold Seal Pack of 14's Capsules.
SOMEZOL 40mg : Cold Form & Cold Seal Pack of 14's Capsules.

STORAGE :
Protect from heat, sunlight & moisture, store below 30°C.
The expiration date refer to the product correctly stored at the required condition.
Patients and healthcare professionals can also report suspected adverse drug reaction at ade@bosch-pharma.com.
Keep out of the reach of children.
To be sold on prescription of a registered medical practitioner only.

ہدایات :
دھوپ، گرمی اور نمی سے محفوظ ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
بچوں کی پہنچ سے دُور رکھیں۔
صرف مستند ڈاکٹر کے نسخے پر فروخت کے لئے۔

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