SOMELINZ

20mg, 40mg Capsules

سومی لِنز کیپسول

(Esomeprazole)

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

ENTERIC COATED PELLETS

DESCRIPTION

The active ingredient in **Somelinz** (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 $(C_{17}H_{18}N_3O_3S)_2Mg \times 3\ H_2O$ with molecular weight of 767.2 as a trihydrate and 713.1 on an anhydrous basis.

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.

COMPOSITION

Somelinz Capsules 20mg : Each Delayed Released Capsule Contains: Esomeprazole Magnesium Trihydrate 22.3mg eq. to Esomeprazole ..... 20mg USP (Enteric Coated Pellets).

Somelinz Capsules 40mg : Each Delayed Released Capsule Contains: Esomeprazole Magnesium Trihydrate 44.5mg eq. to Esomeprazole ..... 40mg USP (Enteric Coated Pellets).

CLINICAL PHARMACOLOGY

Pharmacokinetics

Absorption: Somelinz 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 16L.

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.

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.

INDICATIONS AND USAGE

Gastroesophageal Reflux Disease (GERD)

Healing of Erosive Esophagitis: Somelinz 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 **Somelinz** may be considered.

Maintenance of Healing of Erosive Esophagitis: Somelinz is indicated to maintain symptom resolution and healing of erosive esophagitis.

Symptomatic Gastroesophageal Reflux Disease: Somelinz is indicated for treatment of heartburn and other symptoms associated with GERD.

Risk Reduction of NSAID-Associated Gastric Ulcer: Somelinz 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 **Somelinz**, 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.

Pathological Hypersecretory Conditions Including Zollinger-Ellison Syndrome: Somelinz is indicated for the long-term treatment of pathological hypersecretory conditions, including Zollinger-Ellison Syndrome

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. **Somelinz** Capsules should be swallowed whole and taken at least one hour before eating.

Recommended Dosage Schedule		
Indication	**Dose**	**Frequency**
Gastroesophageal Reflux Disease (GERD)		
Healing of Erosive Esophagitis	20 or 40mg	Once Daily for 4 to 8 Weeks*
*If Esophagitis do not heal, an additional 4 to 8 weeks of treatment may be considered.		
Maintenance of Healing of Erosive Esophagitis	20mg	Once Daily**
**Controlled studies did not extend beyond six months		
Symptomatic Gastroesophageal Reflux Disease	20mg	Once Daily for 4 Weeks***
***If symptoms do not resolve, an additional 4 weeks of treatment may be considered.		
Risk Reduction of NSAID Associated Gastric Ulcer	20 or 40mg	Once Daily for up to 6 months **
**Controlled studies did not extend beyond six months		
Pathological Hypersecretory Conditions Including Zollinger-Ellison Syndrome	40 mg†	‡Twice Daily
†Dosage regimens should be adjusted to individual patient needs . ‡Doses up to 240 mg daily have been administered		

H. pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence		
Drugs	**Dose**	**Frequency**
Triple Therapy		
Somelinz Amoxicillin Clarithromycin	40mg 1000mg 500mg	Once Daily for 10 days Twice Daily for 10 days Twice Daily for 10 days

Paediatric Dosage Schedule (1 to 11 yrs.#)		
Indication	**Dose**	**Frequency**
Short term treatment of symptomatic GERD	10mg	Once Daily for 8 Weeks
Healing of Erosive Esophagitis		
Weight < 20 kg Weight > 20 kg	10mg 10 or 20mg	Once Daily for 8 weeks Once Daily for 8 weeks
#Doses over 1mg / kg / day have not been studied		

Paediatric Dosage Schedule (12 to 17 yrs.)		
Indication	**Dose**	**Frequency**
Short term treatment of GERD	20 or 40mg	Once Daily for 8 Weeks

Pediatric: The safety and effectiveness of **Somelinz** for the treatment of symptomatic GERD in patients <1 year of age have not been established.
The safety and effectiveness of **Somelinz** for other pediatric uses have not been established.
Geriatrics / 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 **Somelinz** should not be exceeded.
Gender : No dosage adjustment is necessary.

CONTRAINDICATIONS
Somelinz is contraindicated in patients with known hypersensitivity to any component of the formulation or to substituted benzimidazoles. Hypersensitivity reactions e.g., angioedema and anaphylactic reaction/shock have been reported.

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. Atrophic gastritis has been noted occasionally in gastric corpus biopsies from patients treated long-term with omeprazole, of which **Somelinz** is an enantiomer.
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 may interfere with the absorption of drugs where gastric pH is an important determinant of bioavailability (eg. ketoconazole, iron salts and digoxin). Patient treated with proton pump inhibitors and warfarin concomitantly may need to be monitored for increases in INR and prothrombin time. Concomitant treatment with a combined inhibitor of CYP2C19 and CYP3A4, such as voriconazole, may result in more than doubling of the esomeprazole exposure. Somelinz may reduce the plasma levels of atazanavir and nelfinavir and increase the plasma levels of saquinavir

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. 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. 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, but greater sensitivity of some older individuals cannot be ruled out.

ADVERSE REACTIONS
In adult patients (above 18yrs incidence > 1%). None found to be dose-related, Like Headache, abdominal pain, diarrhoea, flatulence, nausea/vomiting, constipation, Dermatitis, pruritis, urticaria, dizziness, dry mouth. **Rare:** Hypersensitivity reactions e.g. angioderma, anaphylactic reaction. In peadiatric patients (1-17 yrs incidence > 1-2%): Headache, diarrhoea, abdominal pain, nausea and somnolence.

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.

HOW SUPPLIED
Somelinz 20mg : Pack of 14's Capsules.
Somelinz 40mg : Pack of 14's Capsules.

INSTRUCTIONS
- Protect from light and moisture, store at room temperature.
- Keep out of reach of children.

WARNING: To be sold on prescription of a registered medical practitioner only.

ہدایات :-
روشنی اور نمی سے محفوظ کمرے کے درجہ حرارت پر رکھیں۔
بچوں کی پہنچ سے دور رکھیں۔ ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
انتباہ:۔ صرف رجسٹرڈ میڈیکل پریکٹیشنر کے نسخے پر فروخت کے لیے۔

Manufactured by:
LINZ Pharmaceuticals (Pvt.) Ltd.
Plot No. 31-G & 31-H, Sector 15, K.I.A,
Karachi, Pakistan.