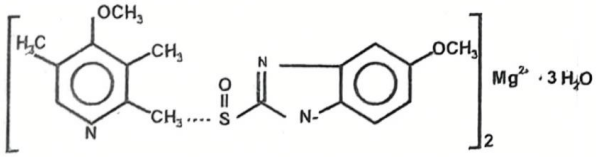
ESOAIM
(Esomeprazole)
20mg, 40mg, Capsules

ایسوائیم (ایسومیپرازول)

DESCRIPTION

ESOAIM capsules is an enteric-coated pellet formulation of esomeprazole magnesium due to its acid labile nature. Esomeprazole is the S-isomer of omeprazole, which inhibits gastric acid secretion more effectively than omeprazole. Chemically it is bis(5-methoxy-2-[(S)-[(4-methoxyR-3, 5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazote-1-yl) magnesium trihydrate. The molecular formula is $(C_{17}H_{18}N_3O_3S)_2Mg \times 3H_2O$ and the structural formula is:



QUALITATIVE AND QUANTITATIVE COMPOSITION

ESOAIM is available for oral administration as:

1. ESOAIM capsules 20mg
   Each capsule contains:
   Enteric-coated pellets of Esomeprazole magnesium trihydrate equivalent to Esomeprazole.....20mg
2. ESOAIM capsules 40mg
   Each capsule contains:
   Enteric-coated pellets of Esomeprazole magnesium trihydrate equivalent to Esomeprazole.....40mg

CLINICAL PHARMACOLOGY

Mechanism of action

Esomeprazole works by binding irreversibly to the H+/K+ ATPase in the proton pump. Because the proton pump is the final pathway for secretion of hydrochloric acid by the parietal cells in the stomach, its inhibition dramatically decreases the secretion of hydrochloric acid into the stomach and alters gastric pH.

Pharmacokinetics

Absorption

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 40mg.

At repeated once-daily dosing with 40mg, 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 40mg 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 intragastric acidity.

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 16L.

Metabolism

Esomeprazole is extensively metabolized in the liver by the cytochrome P-450 (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 part is dependent on. CYP3A4 which forms the sulphone metabolite.

Excretion

Total plasma clearance is about 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 than 1% of the 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 remainings are found as inactive metabolites in the feces.

Special Populations

Geriatric

The AUC and C_{max} 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.

Pediatric

The pharmacokinetics of esomeprazole have not been studied in patients, < 18 years of age.

Hepatic Insufficiency

In patients with mild and moderate hepatic insufficiency, the AUCs were within the range that could be expired 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 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 20mg 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.

THERAPEUTIC INDICATIONS

ESOAIM (Esomeprazole) is indicated for:

1.Gastroesophageal Reflux Disease (GERD)

- Treatment of erosive reflux esophagitis
- Long term management of patients with healed esophagitis to prevent relapse.
- 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 helicobacter pylori infection.
- Prevention of relapse of peptic ulcers in patients with helicobacter pylori associated 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

DOSAGE AND ADMINISTRATION

The recommended adult dosage are outlined in the table below. ESOAIM capsule should be swallowed whole and taken at least one hour before meals.

For patients with severe liver impairment (Child Pugh

Recommended Adult Dosage Schedule		
Indication	Dose	Frequency
1. Gastroesophageal Reflux Disease Healing of erosive esophagus	40 mg or 20mg	once daily 4 to 8 week (an additional 4-8 week treatment may be considered if symptoms persist or esophagitis does not heal)
Maintenance of healing erosive gastroesophageal	20mg	Once daily
Symptomatic Gastroesophageal reflux disease without esophagitis	20mg or 40 mg	Once daily for 4 weeks (an additional 4/8 weeks treatment may be considered if symptoms does not resolve completely.
H. Pylori eradication to reduce the risk of duodenal ulcer Recurrence ESOAIM Amoxicillin Clarithromycin	40mg 1000mg 500mg	Once daily for 10 days Twice daily for 10 days Twice daily for 10 days

Class C), a dose of 20mg of ESOAIM (Esomeprazole) should not be exceeded.

ADVERSE REACTIONS

The following adverse drug reactions have been reported during therapy of esomeprazole. None found to be dose-related.

Common: Headache, abdominal pain, diarrhea, flatulence, nausea/vomiting, constipation.

Uncommon: Dermatitis, pruritis, urticária, dizziness, dry mouth

Rare:- Hypersensitivity reactions e.g. Angioedema, anaphylactic reaction.

The following adverse drug reactions have been observed for the racemate omeprazole and may occur with esomeprazole:

Central and peripheral nervous system: Paraesthesia, somnolence, insomnia, vertigo. Reversible mental confusion, agitation, aggression, depression and hallucinations, predominantly in severely ill patients.

Endocrine: Gynaecomastia.

Gastrointestinal: Stomatitis and gastrointestinal candidiasis.

Haematological: Leukopenia, thrombocytopenia, agranulocytosis and pancytopenia.

Hepatic: Increased liver enzymes, encephalpathy in patients with pre-existing severe liver disease: hepatitis with or without jaundice, hepatic failure.

Skin: Rash, photosensitivity, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN) alopecia.

Other: Malaise, hypersensitivity reactions e.g fever, bronchospasm, interstitial nephritis. Increased sweating, peripheral oedema, blurred vision, taste disturbance and hyponatraemia.

CONTRAINDICATIONS

ESOAIM (Esomeprazole) is contraindicated in patients with known hypersensitivity to drug or 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.

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 occassionally in gastric corpus biopsies from patients treated long-term with omeprazole, of which esomeprazole is an enantiomer.

Patients on-demand treatment should be instructed to contact their physician if their symptoms change in character.

- When prescribing esomeprazole for on-demand therapy, the implications for interactions with other pharmaceutics, due to fluctuating plasma concentrations of esomeprazole should be considered.
- When prescribing esomeprazole for eradication of helicobacter pylori infection possible drug interactions for other components in the triple therapy should be considered.
- Patients with rare hereditary problems of fructose intolerance, Glucose-galactose malabsorption of sucrase-isomaltase insufficiency should not take this medicine.

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 esomeparazole 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 due to the potential for serious adverse reactions in nursing infants from esomeprazole.

Drug Interactions

- In common with the use of other inhibitors of acid secretion or antacids, the absorption of ketoconazole and itraconazole can decrease during treatment with esomeprazole due to decreased intragastric acidity during treatment with esomeprazole.
- Esomeprazole inhibits CYP2C19, the major esomeprazole metabolising enzyme. Thus, when esomeprazole is combined with drugs metabolised by CYP2C19, such as diazepam, citalopram, imipramine, clomipramine, phenytoin etc, the plasma concentrations of these drugs may be increased and a dose reduction could be needed.

STORAGE

Store at room temperature.

Keep out of reach of children.

Manufactured By:
AIMS PHARMACEUTICALS
Plot # 291, Industrial Triangle, Kahuta Road,
Islamabad-Pakistan