JENREX Capsules
(Esomeprazole Magnesium)

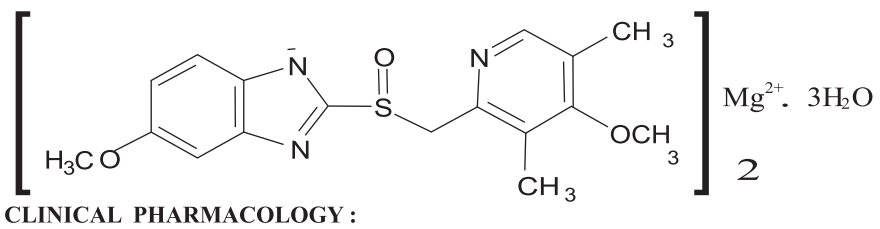
جین ریکس کیپسولز
ایس اومیپرازول میگنیشیم

COMPOSITION:
JENREX 20mg Capsules:
Each Capsule Contains: Esomeprazole Magnesium enteric coated pellets, equivalent to Esomeprazole.....20mg

JENREX 40mg Capsules:
Each Capsule Contains: Esomeprazole Magnesium enteric coated pellets, equivalent to Esomeprazole.....40mg

PHARMACOLOGICAL CLASSIFICATION:
Proton Pump Inhibitor.

DESCRIPTION:
Esomeprazole is the S - isomer of Omeprazole, which is a mixture of S - & R - isomers. Its empirical formula is $(C_{17}H_{18}N_3O_3S)_2$ Mg x 3 H_2O, with a molecular weight of 767.2 as a trihydrate and 713.1 on an anhydrous basis. The structural formula is:



CLINICAL PHARMACOLOGY :
Pharmacokineties:
Absorption: **JENREX** Delayed-released Capsule contains an enteric-coated pellet formulation of Esomperazole (because Esomeprazole is acid-labile) so that absorption of Esomeprazole begins only after the granules leave the stomach. After oral administration, peak plasma levels (Cmax) occur at apporximately 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).
At repeated once daily dosing with 40 mg, the systematic bioavailability is approximately 90% as compared to 64% after a single dose of 40mg. The AUC after administration of a single 40mg dose of **JENREX** is decreased by 43 - 53% after food intake as compared to fasting conditions. **JENREX** should be taken at least one hour before meals.
Distribution: **JENREX** is 97% bound to plasma proteins. Plasma protein binding is constant over the concentration range of 2 - 20 umol/L. The apparent volume of distribution at steady state in healthy volunteers is approximately 16L. **Metabolism:** **JENREX** is extensively metabolized in the liver by the cytochrome P450 (CYP) enzyme system. The metabolites of **JENREX** lack anti-secretory activity. The major part of **JENREX** metabolism is dependent upon the CYP 2 C 19 isoenzyme, which forms the hydroxy and desmethyl metabolites. The remaining amount is dependent on CYP 3A4, which forms the sulphor metabolites.
Excretion: The plasma elimination half-life of **JENREX** is approximately 1 - 1.5 hours. Less than 1% of parent drug is excreted in the urine, Approximately 80%of an oral dose of **JENREX** is excreted as inactive metabolite in the urine,and the remainder is found as inactive metabolite in the feces.
Pharmacokinetics in Geriatrics: 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.
Pharmacokinetics in Pediatrics: The pharmacokinetics of **JENREX** has not been studied in patients less than 18 years of age.
In patients with mild to moderate hepatic insufficiency, the AUCs were within the range that could be expected in patients with normal liver function. No dosage adjustment is recommended for patients with mild to moderate hepatic insufficiency (Child Pugh classes A & B). However, in patients with severe hepatic insufficiency (Child Pugh Class C), a dose of 20mg once daily should not be exceeded.
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 cells. The S - & R - isomers of Omeprazole are protonated and converted in the acidic compartment of the parietal cells forming the active inhibitor, the achiral sulphenamide. By acting specifically on the Proton Pump, Esomeprazole blocks the final steps in acid production thus reducing gastric acidity. This effect is dose-related up to daily dose of 40mg and leads to inhibition of gastric acid secretions.

INDICATIONS AND DOSAGE:
Treatment of Gastroesophageal Reflux Disease (GERD):
Healing of Erosive Esophagitis:

Heartburn and other symptoms associated with GERD:
Tripple Therapy: (JENREX plus Amoxicillin and Clarithromycin): **JENREX** is indicated in combination with Amoxicillin and Clarithromycin for the treatment of patients with H. pylori infection and to eradicate Duodenal Ulcer disease.
CONTRAINDICATIONS:
JENREX Capsules are contraindicated in patients with known hypersensitivity to any component of the formulation.
PRECAUTIONS:
General: Symptomatic response to therapy with **JENREX** does not preclude the presence of gastric malignancy. Atrophic gastritis has been noted occasionally in gastric corpus biopsies from patients treated for long term with **JENREX**
Information for Patient:
JENREX Delayed-Release Capsules should be taken at least one hour before meals.

DRUG INTERACTIONS:
Esomeprazole is extensively metabolized in the liver byCYP2C19 and CYP3A4. Drug interaction studies have shown that Esomeprazole does not have any clinically significant interactions with Phenytoin, Warfarin, Quinidine, Clarithromycin, Amoxicilliin.
Esomeprazole may potentially interfere with CYP2C19, the major Esomeprazole metabolizing enzyme. Co-administration of Esomeprazole 30mg and diazepam,a CYP2C19 substrate, resulted in a 45% decrease in clearance of diazepam. Increased plasma levels of diazepma were observed 12 hours after dosing and onwards. 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).
Combination Therapy with Clarithromycin: Co-administration of Esomeprazole, Clarithromycin and Amoxicillin have resulted in increase in the plasma levels of Esomeprazole and 14-hydroxyclarithromycin.
PREGNANCY:
Teratogenic Effects:
Pregnancy Category B.
PEDIATRIC USE:
Safety and effectiveness in pediatric patients have not been established.

GERIATRIC USE:
No overall difference in safety and efficacy was 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:
Body as a Whole: Abdomen enlarged, allergic reaction, asthenia, back pain, chest pain, substernal, facial edema, peripheral edema, hot flushes, fatigue, fever, flu-like disorder, generalized edema, leg edema, malaise, pain, rigers.
Cardiovascular: Flushing, hypertension, tachycardia.
Endocrine: Goiter.
Gastrointestinal: Bowel irregularity, constipation, aggravated dyspepsia, dysphagia, dysplasia GI, epigastric pain, esophageal disorder, frequent stools, gastroenteritis, GI hemorrhage, hiccup, melena, pharynx disorder, rectal disorder, serum gastrin increased, tongue disorder, tongue edema, ulcerative stomatitis, vomiting.
Hearing: Earache, tinnitus.
Hematologic: Anemia,anemia hypochromic, cervical - lymphadenopathy,epistaxis,leukocytosis,leukopenia, thrombocytopenia.
Hepatic: Bilirubinemia, abnormal hepatic function, SGOT increased, SGPT increased.
Metabolic/Nutritional: Glycosuria, hyperuricemia, hyponatremia, increased alkaline phosphatase, thirst, vitamin B12deficiency, weight increase, weight decrease.
Musculoskeletal: Arthralgia, arthritis aggrevated, arthropathy, cramps, fibromyalgia syndrome, hernia, polymyalgiarheumatica.
Nervous System / Psychiatric: Anorexia, apathy, increased appetite, confusion, depression aggravated, dizziness, hypertonia, nervousness, hypoesthesia, impotence, insomnia, confusion, paresthesia, sleep disorder, somnolence,tremor, vertigo, visual field defect.
Reproductive: Dysmenorrhoea, menstrual disorder.
Respiratory: Aggravated asthma, coughing, dyspnea, larynx edema, pharyngitis, rhinitis, sinusitis.
Visual: Conjunctivitis, abnormal vision.
Combination Treatment with Amoxicillin and Clarithromycin: In clinical trial using combination therapy with **JENREX** plus Amoxicillin and Clarithromycin, no adverse events peculiar to these drug combinations were observed.Adverse events that occurred have been limited to those that had been observed with either **JENREX** Amoxicillin, or Clarithromycin alone, The most frequently reported drug- related adverse events for patients who received tripple therapy for 10 days were diarrhea, taste perversion and abdominal pain, No treatment-emergent adverse events were observed at higher rates with tripple therapy than were observed with **JENREX** alone.

DOSAGE AND ADMINISTRATION:
The recommended adult dosages are outlined in the table below. **JENREX** Delayed-Release Capsules should be swallowed whole and taken at least one hour before meal. For patients who have difficulty in swallowing capsules, one tablespoon of applesauce can be added to an empty bowl and the **JENREX** Delayed-Release Capsule can be opened, and the pellets inside the capsules 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. The pellets have also been shown in vitro to remain intact when exposed to tap water, orange juice, apple juice and yogurt.

Recommended Adults Dosage Schedule of JENREX

Indication	Dose	Frequency
Gastroesophageal Reflux Disease (GERD) • Healing of Erosive Esophagitis	20/40mg	Once Daily for 4 to 8 weeks
H. pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence: Tripple Therapy: **JENREX** Amoxicillin Clarithromycin	 20/40mg 1000 mg 500 mg	 Twice Daily for 10 Days Twice Daily for 10 Days Twice Daily for 10 Days

* The majority of patients are healed within 4 to 8 weeks. For patients who do not heal after 4-8 weeks, an additional 4-8 weeks of treatment may be considered.

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).

Gender: No dosage adjustment is necessary.

STORAGE INSTRUCTIONS:
Store in a cool, dry place below 30°C. Keep out of reach of children.

PRESENTATION:
JENREX 20mg:
Two blister strips of seven capsules each, in packing of 14 Capsules.

JENREX 40mg:
Two blister strips of seven capsules each, in packing of 14 Capsules.

خوراک:
ڈاکٹر کی ہدایت کے مطابق استعمال کریں

ہدایات:
دوا کو ۳۰ ڈگری سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
دھوپ اور نمی سے بچائیں۔ بچوں کی پہنچ سے دُور رکھیں۔

JENNER
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JENNER PHARMACEUTICALS (Pvt) Ltd.
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