ESOFLUX® 40 mg

Esomeprazole Magnesium
capsules

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
* Keep this leaflet. You may need to read it again.
* If you have any further questions, ask your doctor or pharmacist.
* This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
* If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 11.

1.DESCRIPTION
ESOFLUX® is a capsule containing enteric coated pellets.

2. COMPOSITION
Each capsule contains:
40 mg of Esomeprazole Magnesium Trihydrate present in 470,6mg of enteric coated pellets.
Excipients: Hypromellose E5, Polysorbate 80 (Tween-80), Sodium Hydroxide, Purified Talc, Titanium dioxide, Methacrylic Acid & Ethyl Acrylate copolymer (Type C) L30D, Diethyl phthalate.

3. THERAPEUTIC INDICATIONS
ESOFLUX® is indicated in adults (18 years of age and above) for treatment of conditions where a reduction in gastric acid secretion is required such as:
• Treatment of gastroesophageal reflux disease (GERD).
• Risk reduction of NSAID-associated gastric ulcer.
• H. pylori eradication to reduce the risk of duodenal ulcer recurrence.
• Pathological hypersecretory conditions, including Zollinger-Ellison syndrome.

4. MECHANISM OF ACTION AND PHARMACODYNAMIC EFFECTS
Esomeprazole magnesium (a substituted benzimidazole), reduces gastric acid secretion through a highly targeted mechanism of action.
Esomeprazole accumulates in the acidic environment of the parietal cells after absorption, where it is converted into the active form. This active sulphenamide specifically binds the H+, K+ -ATPase (proton pump), to block the final step in acid production by the parietal cells, thus reducing gastric acidity.
Esomeprazole is effective in the inhibition of both basal acid secretion and stimulated acid secretion.

5. PHARMACOKINETICS
Absorption
ESOFLUX® Capsules contain an enteric-coated pellet formulation of esomeprazole. 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 40 mg. The mean exposure (AUC) to esomeprazole increases from 4.32 µmol*hr/L on day 1 to 11.2 µmol*hr/L on day 5 after 40 mg once daily dosing.
The AUC after administration of a single 40 mg dose of ESOFLUX® capsules is decreased by 43% to 53% after food intake compared to fasting conditions. ESOFLUX® 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 to 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 CYP 2C19 isoenzyme, which forms the hydroxy and desmethyl metabolites.
The remaining amount is dependent on CYP 3A4 which forms the sulphone metabolite. CYP 2C19 isoenzyme exhibits polymorphism in the metabolism of esomeprazole, since some 3% of Caucasians and 15 to 20% of Asians lack CYP 2C19 and are termed Poor Metabolizers. At steady state, the ratio of AUC in Poor Metabolizers to AUC in the rest of the population (Extensive Metabolizers) is approximately 2. Following administration of equimolar doses, the S- and R-isomers are metabolized differently by the liver, resulting in higher plasma levels of the S- than of the R-isomer.

Excretion
The plasma elimination half-life of esomeprazole is approximately 1 to 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.

6. CONTRAINDICATIONS
• In patients who are hypersensitive to esomeprazole or to any ingredient in the formulation.
• With co-administration of rilpririvine due to significant decrease in rilpivirine exposure and loss of therapeutic effect.

7. DOSAGE AND ADMINISTRATION
Gastroesophageal Reflux Disease (GERD)
For Adults: ESOFLUX® 40 mg Once daily for 4 to 8 weeks.
For 12 to 17 years: ESOFLUX® 40 mg Once daily for up to 8 weeks.

Risk Reduction of NSAID-Associated Gastric Ulcer
ESOFLUX® 40 mg Once daily for up to 6 months.

H. pylori Eradication (Triple Therapy)
ESOFLUX® 40 mg Once daily for 10 days.
Amoxicillin 1000 mg Twice daily for 10 days.
Clarithromycin 500 mg Twice daily for 10 days.

Pathological Hypersecretory Conditions
ESOFLUX® 40 mg Twice daily.
Patients with severe liver impairment-do not exceed dose of 20 mg.

8. WARNINGS AND PRECAUTIONS
• Symptomatic response does not preclude the presence of gastric malignancy.
• Atrophic gastritis has been noted with long-term omeprazole therapy
• Acute interstitial nephritis has been observed in patients taking PPIs.
• Cyanocobalamin (vitamin B-12) Deficiency: Daily long-term use (e.g., longer than 3 years) may lead to malabsorption or a deficiency of cyanocobalamin.
• PPI therapy may be associated with increased risk of Clostridium difficile associated diarrhea.
• Bone Fracture: Long-term and multiple daily dose PPI therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist or spine.
• Hypomagnesemia has been reported rarely with prolonged treatment with PPIs.
• Avoid concomitant use of ESOFLUX® with St John's Wort or rifampin due to the potential reduction in esomeprazole levels.
• Interactions with diagnostic investigations for Neuroendocrine Tumors: Increases in intragastric pH may result in hypergastrinemia and enterochromaffin-like cell hyperplasia and increased chromogranin A levels which may interfere with diagnostic investigations for neuroendocrine tumors.

9. SPECIFIC PATIENT POPULATIONS
Renal Insufficiency: No dose adjustment is required.
Hepatic Insufficiency: No dose adjustment is required for patients with mild to moderate hepatic impairment. The daily doses of 20 mg in patients with severe hepatic impairment should not, as a rule, be exceeded.

Elderly Patients: No dose adjustment is required.

Pregnant Women: There are no adequate or well-controlled studies in pregnant women. Therefore, the safety of ESOFLUX® in pregnancy has not been established. ESOFLUX® should not be administered to pregnant women unless the expected benefits outweigh the potential risks. Pregnancy Category B.

Nursing Women: It has not been investigated whether or not esomeprazole is excreted in human breast milk. No studies in lactating women have been performed. Precaution should be exercised because many drugs can be excreted in human milk. Esomeprazole is the S-isomer of omeprazole, which is secreted in breast milk. Therefore, ESOFLUX® should not be given to nursing mothers unless its use is considered essential.

10. DRUG INTERRACTIONS
Esomeprazole is extensively metabolized in the liver by CYP2C19 and CYP3A4.
• May affect plasma levels of antiretroviral drugs – use with atazanavir and nelfinavir is not recommended; if saquinavir is used with ESOFLUX®, monitor for toxicity and consider saquinavir dose reduction.
• May interfere with drugs for which gastric pH affects bioavailability (e.g., ketoconazole, iron salts, erlotinib, digoxin and mycophenolate mofetil). Patients treated with ESOFLUX® and digoxin may need to be monitored for digoxin toxicity.
• Combined inhibitor of CYP 2C19 and 3A4 may raise esomeprazole levels.
• Clopidogrel: ESOFLUX® decreases exposure to the active metabolite of clopidogrel.
• May increase systemic exposure of cilostazol and an active metabolite. Consider dose reduction.
• Tacrolimus: ESOFLUX® may increase serum levels of tacrolimus.
• Methotrexate: ESOFLUX® may increase serum levels of methotrexate.

11. ADVERSE REACTIONS
Most common adverse reactions:
• Adults (≥ 18 years) (incidence > 1%) are headache, diarrhea, nausea, flatulence, abdominal pain, constipation, and dry mouth.
• Pediatric (12 to 17 years) (incidence > 2%) are headache, diarrhea, abdominal pain, nausea, and somnolence.

12. STORAGE CONDITION
Store below 30° C. Protect from light.
Keep in original pack in intact condition.

Marketing Authorisation Holder, Manufacturer
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ESOFLUX® 40 mg, 30 capsules Reg. N°: 124024/1

This is a medicine:
- A medicine is a product which affects your health and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who dispensed the medicine.
- The doctor and the pharmacist are the experts in medicine, their benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.
- Keep all medicine out of reach of children.

Council of Arab Health Ministers
Union of Arab pharmacists

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