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Rx

ESOMEPRAZOLE

EMEP

40 mg Lyophilized Powder for Injection (I.V.)
Proton Pump Inhibitor

FORMULATION:
Each vial contains:
Esomeprazole .....40 mg
(as Sodium)

PRODUCT DESCRIPTION:
White to almost white lyophilized cake. After reconstitution with 0.9% sodium chloride solution it yields clear and almost colorless solution, free from any visible particles.

PHARMACODYNAMICS:
Esomeprazole is the S-isomer of omeprazole, which is a mixture of the S- and R- isomers. Esomeprazole is a proton pump inhibitor. It suppresses secretion of gastric acid by inhibiting the enzyme system of hydrogen / potassium adenosine triphosphatase (H^+/K^+ ATPase), the 'proton pump' of the gastric parietal cell. An almost white lyophilized cake.

PHARMACOKINETICS:
Esomeprazole is rapidly absorbed after oral doses, with peak plasma levels occurring after about 1 to 2 hours. It is acid labile and an enteric-coated formulation has been developed. Bioavailability of esomeprazole increases with both dose and repeated administration to about 68 and 89% for doses of 20 and 40 mg respectively. Food delays and decreases the absorption of esomeprazole, but this does not significantly change its effect on intragastric acidity. Esomeprazole is about 97% bound to plasma proteins. It is extensively metabolized in the liver by the cytochrome P450 isoenzyme CYP2C19 to hydroxy and desmethyl metabolites, which have no effect on gastric acid secretion. The remainder is metabolised by the cytochrome P450 isoenzyme CYP3A4 to esomeprazole sulfone. With repeated dosage, there is a decrease in first-pass metabolism and systemic clearance, probably caused by an inhibition of the CYP2C19 isoenzyme. However, there is no accumulation during once daily use. The plasma elimination half-life is about 1.3 hours. Almost 80% of an oral dose is eliminated as metabolites in the urine, the remainder in the faeces.

INDICATIONS:
Esomeprazole is indicated in the treatment of peptic ulcer disease and NSAID-associated ulceration, in gastro-oesophageal reflux disease (GERD) and the Zollinger-Ellison syndrome.

CONTRAINDICATIONS:
There have been well documented reports of individuals with a history of penicillin hypersensitivity reactions that have experienced severe hypersensitivity reactions when treated with a cephalosporin. Before initiating therapy with any penicillin, careful inquiry should be made concerning previous hypersensitivity reactions to penicillins, cephalosporins, and other allergens. If an allergic reaction occurs, amoxicillin should be discontinued and the appropriate therapy instituted.

Serious anaphylactic reactions require immediate emergency treatment with epinephrine, oxygen, intravenous steroids, and airway management, including intubation, should also be administered as indicated.

Pseudomembranous colitis has been reported with nearly all antibacterial agents, including clarithromycin and amoxicillin, and may range in severity from mild to life threatening. Therefore, it is important to consider this diagnosis in patients who present with diarrhea subsequent to the administration of antibacterial agents.

DRUG INTERACTIONS:
Esomeprazole is extensively metabolized in the liver by CYP2C19 and CYP3A4. In vitro and in vivo studies have shown that esomeprazole is not likely to inhibit CYPs 1A2, 2A6, 2C9, 206, 2E1 and 3A4. No clinically relevant interactions with drugs metabolized by these CYP enzymes would be expected. Drug interaction studies have shown that esomeprazole does not have any clinically significant interactions with phenytoin, warfarin, quinidine, clarithromycin or amoxicillin. Post-marketing reports of changes in prothrombin measures have been received among patients on concomitant warfarin and esomeprazole therapy. Increases in INR and prothrombin time may lead to abnormal bleeding and even death. Patients treated with proton pump inhibitors and warfarin concomitantly may need to be monitored for increases in INR and prothrombin time. Esomeprazole may potentially interfere with CYP2C19, the major esomeprazole metabolizing enzyme. Coadministration of esomeprazole 30 mg and diazepam, a CYP2C19 substrate, resulted in a 45% decrease in clearance of diazepam. Increased plasma levels of diazepam were observed 12 hours after dosing and onwards. However, at that time, the plasma levels of diazepam were below the therapeutic interval, and thus this interaction is unlikely to be of clinical relevance.

Esomeprazole inhibits gastric acid secretion. 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).

Coadministration of oral contraceptives, diazepam, phenytoin, or quinidine did not seem to change the pharmacokinetic profile of esomeprazole.

Co-administration of esomeprazole, clarithromycin, and amoxicillin has resulted in increases in the plasma levels of esomeprazole and 14-hydroxyclarithromycin.

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 regnancy only if clearly needed.

There are no adequate and well-controlled studies in pregnant women. Sporadic reports have been received of congenital abnormalities occurring in infants born to women who have received esomeprazole during pregnancy.

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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, because of the potential for serious adverse reactions in nursing infants from esomeprazole, and because of the potential for tumorigenicity shown for omeprazole in rat carcinogenicity studies, 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 EFFECTS:
All medicines may cause side effects, but many people have no, or minor, side effects. Check with your doctor if any of these most COMMON side effects persist or become bothersome when using esomeprazole IV. Constipation; diarrhea; drowsiness; dry mouth; gas; headache; nausea; pain, swelling, or redness at the injection site; stomach pain. Seek medical attention right away if any of these SEVERE side effects occur when using Esomeprazole I.V.: Severe allergic reactions (rash; hives; itching; difficulty breathing; tightness in the chest; swelling of the mouth, face, lips, or tongue; unusual hoarseness); bone pain; chest pain; dark urine; fast heartbeat; fever, chills, or sore throat; red, swollen, blistered, or peeling skin; severe diarrhea; severe stomach cramps or pain; unusual bruising or bleeding; unusual tiredness.

Reporting of Suspected Adverse Reactions:
To allow continued monitoring of the benefit/risk balance of the medicinal product, reporting of suspected adverse reaction is necessary. Healthcare professionals are encouraged to report any suspected adverse reactions directly to the importer/distributor and/or report to FDA: www.fda.gov.ph.
Patients are advised to seek immediate medical attention at first sign/s of adverse reactions.

DOSAGE AND ADMINISTRATION:
The treatment of Gastroesophageal Reflux Disease (GERD) and NSAID associated ulceration and the Zollinger-Ellison syndrome is with 20 mg or 40 mg esomeprazole given once daily by intravenous injection (no less than 3 minutes) or intravenous infusion (10 to 30 minutes).

Doses of esomeprazole may need to be reduced in patients with hepatic impairment history of erosive esophagitis for more than 10 days have not been demonstrated.

Administration in children.
UK licensed product information allows for the use of adult doses of esomeprazole in children over 12 years. In the USA licensed doses, which may be given once daily for up to 8 weeks for the treatment of gastro-oesophageal reflux in children, are:
• 1 to 11 years: 10 mg
• 12 to 17 years: 20 or 40 mg

For healing erosive oesophagitis in children, the following doses based on body-weight are licensed in the USA to be given once daily for up to 8 weeks:
• less than 20 kg: 10 mg
• 20 kg or over: 10 or 20 mg

Administration in hepatic impairment. No dosage adjustment of esomeprazole is considered necessary for patients with mild to moderate hepatic impairment (Child-Pugh Classes A and B, respectively). For patients with severe hepatic impairment (Child-Pugh Class C), a daily dose of 20 mg should not be exceeded.

Administration in renal impairment. Although no dosage adjustment is considered necessary in patients with renal impairment, UK licensed product information advises caution in those with severe renal impairment, as experience in these patients is limited.

PREPARATION FOR USE:
The powder should be reconstituted with 5 mL of 0.9% Sodium Chloride Injection. Withdraw 5 mL of the reconstituted solution and administered as slow intravenous injection over no less than 3 minutes or by intravenous infusion over 10 to 30 minutes.

The reconstituted solution should be stored at room temperature not exceeding 30°C and should be administered within 12 hours after reconstitution. No refrigeration is required.

OVERDOSE AND TREATMENT:
In the case of overdose/aggravated symptoms, appropriate monitoring and management of the patient should be implemented.

CAUTION:
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

STORAGE CONDITION:
Store at temperatures not exceeding 30°C.

AVAILABILITY:
USP Type-I Clear Glass Vial + Clear Glass Ampoule containing 5mL 0.9% Sodium Chloride (as Diluent) in a box.

FDA Registration No. : DRP-4615
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Manufactured by:
ARISTOPHARMA LTD.
Plot # 14-22, Road # 11 & 12, Shampur-Kadamtali I/A.
Dhaka-1204, Bangladesh.

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SAHAR INTERNATIONAL TRADING INC.
354 Aguirre Ave, Phase III, BF Homes
Parañaque City.
SAHAR

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