Front

Espra®

(Esomeprazole)

Sachet

Peppermint Flavor

ایسپرا

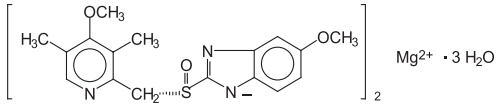
COMPOSITION:
Espra Sachet 20 mg:
Each sachet contains:
Enteric coated pellets of Esomeprazole Magnesium Trihydrate equivalent to Esomeprazole ..... 20 mg.

Product Specs.: Innovator

Espra Sachet 40 mg:
Each sachet contains:
Enteric coated pellets of Esomeprazole Magnesium Trihydrate equivalent to Esomeprazole ..... 40 mg.

Product Specs.: Innovator

DESCRIPTION:
Each **Espra** sachet contains 20 mg or 40 mg of esomeprazole as esomeprazole magnesium in the form of pellets. Esomeprazole is the S-isomer of omeprazole, which inhibits gastric acid secretion more effectively than omeprazole. The esomeprazole granules and inactive granules are constituted with water to form a suspension and are given by oral, nasogastric, or gastric administration. Chemically it is bis (5-methoxy-2-[(S)-[(4-methoxy-3,5-dimethyl-2-pyridinyl) methyl] sulfinyl]-l H•benzimidazole-1-yl) magnesium trihydrate. Its empirical formula is (C11H,•N,O,S)2mg. 3H,O.



CLINICAL PHARMACOLOGY:
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 40 mg.

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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 mg 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.
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 intragastric acidity.
Distribution: Esomeprazole is 97% bound to plasma proteins. Plasma protein binding is constant over the concentration range of 2-20µmol/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 part is dependent on CYP3A4 which forms the sulphone metabolite.
Excretion: Total plasma clearence 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 remainder is 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.
Gender: The AUC and C_{max} values were slightly higher (13%) in females than in males at steady state. Dose adjustment based on gender 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 dose 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 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.

INDICATIONS:
1. *Treatment of gastroesophageal reflux disease (GERD):*
- Healing of Erosive Esophagitis.
- Maintenance of Healing of Erosive Esophagitis.
- Symptomatic Gastroesophageal Reflux Disease.

2. *Risk reduction of nsaid-associated gastric ulcer.*
3. *H. Pylori eradication to reduce the risk of duodenal ulcer recurrence:*
- As a triple therapy (Esomeprazole plus amoxicillin and clarithromycin) is indicated for the treatment of patients with H. pylori infection and duodenal ulcer disease to eradicate H. pylori. Eradication of H. pylori has been shown to reduce the risk of duodenal ulcer recurrence.

Note: 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.
4. *Pathological hypersecretory conditions including zollinger ellison syndrome gastroesophageal reflux disease (GERD):*

DOSAGE AND ADMINISTRATION:
The recommended adult dosages are outlined in the table below. Espra sachet should be taken at least one hour before meals.

Recommended Adult Dosage Schedule		
Indication	**Dose**	**Frequency**
I. Gastroesophageal Reflux Disease (GERD)		
Healing of Erosive Esophagitis	20 mg or 40 mg	Once Daily for 4 to 8 weeks
Maintenance of Healing of Erosive Esophagitis	20 mg	Once Daily
Symptomatic Gastroesophageal Reflux Disease	20 mg	Once Daily for 4 Weeks (If symptoms do not resolve completely after 4 weeks, an additional 4 weeks of treatment may be considered).
II. Risk Reduction of NSAID-Associated Gastric Ulcer	20 mg or 40 mg	Once Daily for up to 6 months
III. H. pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence (Triple Therapy):		
Nexum	40 mg	Once Daily for 10 Days
Amoxicillin	1000 mg	Twice Daily for 10 Days
Clarithromycin	500 mg	Twice Daily for 10 Days
IV. Pathological Hypersecretory Conditions Including Zollinger-Ellison Syndrome	40 mg	Twice Daily

Back

Pediatric (12 to 17 year Olds)		
Indication	**Dose**	**Frequency**
I. Gastroesophageal Reflux Disease (GERD)		
Healing of Erosive Esophagitis	20 mg or 40 mg	Once Daily for 4 to 8 weeks
Symptomatic Erosive (GRED)	20 mg	Once Daily for 4 weeks

For patients with severe liver impairment (Child Pugh Class C), a dose of 20 mg of Espra (Esomeprazole) should not be exceeded.

ADVERSE REACTIONS:
The following adverse drug reactions have been reported during therapy of esomeprazole.
Common: Headache, abdominal pain, constipation, diarrhea, flatulence and nausea/vomiting.
Uncommon: Peripheral oedema, insomnia, dizziness, paraesthesia, somnolence, vertigo, dry mouth, increased liver enzymes, dermatitis, pruritus, rash, urticaria, fracture of the hip and wrist or spine.
Rare: Leukopenia, thrombocytopenia, hypersensitivity reactions e.g. fever, angioedema and anaphylactic reaction/shock, hyponatremia, agitation, confusion, depression, blurred vision, bronchospasm, hepatitis with or without jaundice, alopecia, photosensitivity, arthralgia, myalgia, malaise, increased sweating, stomatitis and gastrointestinal candidiasis.

CONTRAINDICATIONS: Esomeprazole is contraindicated in patients with known hypersensitivity to Proton Pump Inhibitor or substituted benzimidazoles or any excipient of the product. Esomeprazole should not be used concomitantly with nelfinavir.

DRUG INTERACTIONS:
- Co-administration of atazanavir with proton pump inhibitors is expected to substantially decrease atazanavir plasma concentrations and may result in a loss of therapeutic effect and the development of drug resistance.
- Co-administration of saquinavir with proton pump inhibitors is expected to increase saquinavir concentrations, which may increase toxicity and require dose reduction.
- 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 metabolizing enzyme. Thus, when esomeprazole is combined with drugs metabolized 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.
- Drug-induced decrease in gastric acidity results in enterochromaffin like cell hyperplasia and increased Chromogranin A levels which may interfere with investigations for neuroendocrine tumors.
- Concomitant administration of esomeprazole and tacrolimus may increase the serum levels of tacrolimus.
- Co-administration of esomeprazole, clarithromycin, and amoxicillin has resulted in increases in the plasma levels of esomeprazole and 14-hydroxyclarithromycin.
- Avoid concomitant use of Esomeprazole with clopidogrel, St John's Wort, or rifampin.
- Concomitant administration of PPIs and methotrexate may elevate and prolong serum levels of methotrexate and/or its metabolite hydroxymethotrexate.

OVERDOSAGE:
Symptoms: The symptoms with deliberate overdose are transient. Single doses of 80 mg of esomeprazole were uneventful.
Treatment: 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 overdosage, treatment should be symptomatic and supportive.

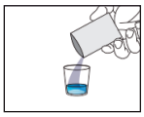
PRECAUTIONS:
General: Symptomatic response to therapy with Esomeprazole does not preclude the presence of gastric malignancy.
- Atrophic gastritis has been noted occasionally in gastric corpus biopsies from patients treated long-term with omeprazole, of which esomeprazole is an enantiomer.
- Proton pump Inhibitor may be associated with an increased risk of Clostridium difficile associated diarrhea, especially in hospitalized patients.
- Proton pump inhibitor (PPI) therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine. Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.
- For patients expected to be on prolonged treatment or who take PPIs with medications such as digoxin or drugs that may cause hypomagnesemia (e.g., diuretics), monitoring magnesium levels prior to initiation of PPI treatment and periodically is required.

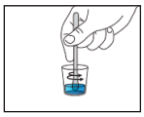
Pregnancy: There are no adequate and well-controlled studies in pregnant women. Esomeprazole should be used during pregnancy only if clearly needed.
Nursing mothers: Because esomeprazole is likely to be excreted in human milk, because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account importance of the drug to the mother.

HOW TO MIX AND ADMINISTER: Prepared in just minutes, once a day.
For oral administration: *Simply mix packet contents with water* to prepare Espra sachet:*
1. ***Add the appropriate amount of water* for the prescribed dose to a container:***
   - 5 mL of water for the 2.5-mg or 5-mg doses
     5 mL = 1 teaspoon
   - 15 mL of water* for the 20-mg, or 40-mg doses
     15 mL = 1 tablespoon
2. *Espra Sachet can be mixed with applesauce. Use with other foods is not recommended.
   Doses for infants and children may range from 2.5 mg to 40 mg. Adult doses may be 20 mg or 40 mg.
3. Empty the contents of a foil packet of Espra Sachet containing the dose prescribed by the doctor into the container of water.
4. Stir and leave 2 to 3 minutes to thicken.
5. Stir again and drink the dose within 30 minutes.

DIRECTIONS FOR USE:

سسپنشن بنانے کا طریقہ:





Espra for 20 mg: →

Empty the sachet content into a small cup containing 2 tablespoons (30 ml) of water to form suspension.

سسپنشن بنانے کیلئے پاؤڈر کو ۲ کھانے کے چمچ (۳۰ ملی لیٹر) پانی میں حل کریں۔

Mix

ملائیں

- Leave 2-3 minutes to thicken, then stir and administration within 30 minutes.
- Refill cup with water and drink.
- Do not use other liquids or foods.

- گاڑھا ہونے کیلئے ۲-۳ منٹ چھوڑیں، پھر ملائیں اور ۳۰ منٹ کے اندر اندر پی لیں۔
- کپ میں دوبارہ پانی بھریں اور پی لیں۔
- پانی کے علاوہ کسی اور شے کے ساتھ استعمال نہ کریں۔

Espra for 40 mg: →

Empty the sachet content into a small cup containing 4 tablespoons (60 ml) of water to form suspension.

سسپنشن بنانے کیلئے پاؤڈر کو ۴ کھانے کے چمچ (۶۰ ملی لیٹر) پانی میں حل کریں۔

If medicine is not used within 30 minutes, throw away the dose and mix a new one. If any medicine remains after drinking, add more water, stir, and make sure the dose is taken right away. For young children, you can give the dose with an oral syringe. Rinse the oral syringe with water after each use.
For administration through a nasogastric (NG) or gastric tube:
- Can be prepared for administration into an NG or gastric tube in just minutes

Please see the Medication Guide in the full Prescribing Information for administration details.

INSTRUCTIONS:
- Store below 30°C.
- Protect from heat, sunlight & moisture.
- Keep out of the reach of children.
- To be sold on the prescription of a registered medical practitioner only.

ہدایات:
۳۰ درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گرمی، دھوپ اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔
صرف مستند ڈاکٹر کے نسخہ پر فروخت کریں۔

PRESENTATION:

ESPRA Sachet 20 mg	:	Pack of 14 sachets.
ESPRA Sachet 40 mg	:	Pack of 14 sachets.

Manufactured by:
Bio-Mark Pharmaceuticals
Plot No. 527, Sundar Industrial Estate, Lahore, Pakistan.

FOR FURTHER INFORMATION PLEASE CONTACT.

CCL

Manufactured for:
CCL Pharmaceuticals (Pvt.) Ltd.
62 Industrial Estate, Kot Lakhpat, Lahore, Pakistan.