ESOLINDA

Instructions for the medicinal product

Trade name: Esolinda.
International Nonproprietary Name: Esomeprazole.
Dosage form: Enteric coated tablets.
Composition:
Esolinda 20 mg: Each enteric coated tablet contains:
Esomeprazole Magnesium USP (As Trihydrate) eq. to Esomeprazole 20 mg.
Approved colours used in coating

Esolinda 40 mg: Each enteric coated tablet contains:
Esomeprazole Magnesium USP (As Trihydrate) eq. to Esomeprazole 40 mg.
Approved colours used in coating
Pharmacotherapeutic group: Proton-pump Inhibitor.
ATC Code: A02BC05.
Pharmacologic property:
Pharmacodynamics:
Esomeprazole is the S-isomer of omeprazole and reduces gastric acid secretion through a specific targeted mechanism of action. It is a specific inhibitor of the acid pump in the parietal cell. Both the R- and S-isomer of omeprazole have similar pharmacodynamic activity. Esomeprazole is a weak base and is concentrated and converted to the active form in the highly acidic environment of the secretory canaliculi of the parietal cell, where it inhibits the enzyme H+K+-ATPase – the acid pump and inhibits both basal and stimulated acid secretion.
After oral dosing with esomeprazole 20 mg and 40 mg the onset of effect occurs within one hour. After repeated administration with 20 mg esomeprazole once daily for five days, mean peak acid output after pentagastrin stimulation is decreased 90% when measured 6–7 hours after dosing on day five.
Pharmacokinetics:
Esomeprazole is acid labile and is administered orally as enteric coated tablets. In vivo conversion to the R-isomer is negligible. Absorption of esomeprazole is rapid, with peak plasma levels occurring approximately 1-2 hours after dose. The absolute bioavailability is 64% after a single dose of 40 mg and increases to 89% after repeated once daily administration. For 20 mg esomeprazole the corresponding values are 50% and 68%, respectively. The apparent volume of distribution at steady state in healthy subjects is approximately 0.22 L/kg body weight. Esomeprazole is 97% plasma protein bound.
Food intake both delays and decreases the absorption of esomeprazole although this has no significant influence on the effect of esomeprazole on intragastric acidity.
Esomeprazole is completely metabolised by the cytochrome P450 system (CYP). The major part of the metabolism of esomeprazole is dependent on the polymorphic CYP2C19, responsible for the formation of the hydroxy- and desmethyl metabolites of esomeprazole. The remaining part is dependent on another specific isoform, CYP3A4, responsible for the formation of esomeprazole sulphone, the main metabolite in plasma.
The major metabolites of esomeprazole have no effect on gastric acid secretion. Almost 80% of an oral dose of esomeprazole is excreted as metabolites in the urine, the remainder in the faeces. Less than 1% of the parent drug is found in urine.
Indications for use:
• Gastroesophageal reflux disease (GORD): Treatment of erosive reflux oesophagitis, Long-term management of patients with healed oesophagitis to prevent relapse, Symptomatic treatment of gastroesophageal reflux disease (GORD);
• In combination with appropriate antibacterial therapeutic regimens for the eradication of Helicobacter pylori: Healing of Helicobacter pylori associated duodenal ulcer, prevention of relapse of peptic ulcers in patients with Helicobacter pylori associated ulcers;
• Patients requiring continued NSAID therapy: Healing of gastric ulcers associated with NSAID therapy, Prevention of gastric and duodenal ulcers associated with NSAID therapy, in patients at risk, Prolonged treatment after IV induced prevention of rebleeding of peptic ulcers.
• Treatment of Zollinger Ellison Syndrome;
Adolescents from the age of 12 years:
•Gastro-Oesophageal Reflux Disease (GORD): treatment of erosive reflux oesophagitis, long-term management of patients with healed oesophagitis to prevent relapse, symptomatic treatment of gastro-oesophageal reflux disease (GORD).
•In combination with antibiotics in treatment of duodenal ulcer caused by Helicobacter pylori.
Contraindications:
• Known hypersensitivity to esomeprazole, substituted benzimidazoles or any other constituents of the formulation;
• Hereditary fructose intolerance, glucose-galactose malabsorption;
• Children younger than 12 years since no data is available. Adolescents from the age of 12 years for another indications except Gastroesophageal Reflux Disease (GORD);
• Should not be used concomitantly with atazanavir and nelfinavir.
Precautions: Due to limited experience in patients with severe renal insufficiency, such patients should be treated with caution.
Pregnancy and Nursing Mother:
Caution should be exercised when prescribing to pregnant women. It is not known whether esomeprazole is excreted in human breast milk. No studies in lactating women have been performed. Therefore Esolinda should not be used during breast-feeding.
Dosage and directions for use:
The tablets should be swallowed whole with liquid. The tablets should not be chewed or crushed. For patients who have difficulty in swallowing, the tablets can also be dispersed in half a glass of non-carbonated water. No other liquids should be used as the delayed release may be dissolved. Stir until the tablets disintegrate and drink the liquid with the pellets immediately or within 30 minutes. Rinse the glass with half a glass of water and drink. The pellets must not be chewed or crushed.
For patients who cannot swallow, the tablets can be dispersed in non-carbonated water and administered through a gastric tube. It is important that the appropriateness of the selected syringe and tube is carefully tested.
Administration through gastric tube:

1. Put the tablet into an appropriate syringe and fill the syringe with approximately 25 ml water and approximately 5 ml air. For some tubes, dispersion in 50 mL water is needed to prevent the pellets from clogging the tube.
2. Immediately shake the syringe for approximately 2 minutes to disperse the tablet.
3. Hold the syringe with the tip up and check that the tip has not clogged.
4. Attach the syringe to the tube whilst maintaining the above position.
5. Shake the syringe and position it with the tip pointing down. Immediately inject 5–10 mL into the tube. Invert the syringe after injection and shake (the syringe must be held with the tip pointing up to avoid clogging of the tip).
6. Turn the syringe with the tip down and immediately inject another 5–10 mL into the tube. Repeat this procedure until the syringe is empty.
7. Fill the syringe with 25 mL of water and 5 mL of air and repeat step 5 if necessary to wash down any sediment left in the syringe. For some tubes, 50 mL water is needed.

Adults and adolescents from the age of 12 years.
Gastro-oesophageal Reflux Disease (GORD) - Treatment of erosive reflux oesophagitis - 40 mg once daily for 4 weeks.
An additional 4 weeks treatment is recommended for patients in whom oesophagitis has not healed or who have persistent symptoms.
Long-term management of patients with healed oesophagitis to prevent relapse - 20 mg once daily.
Symptomatic treatment of gastro-oesophageal reflux disease (GORD) - 20 mg once daily in patients without oesophagitis. If symptom control has not been achieved after four weeks, the patient should be further investigated. Once symptoms have resolved, subsequent symptom control can be achieved using 20 mg once daily. In adults, an on demand regimen taking 20 mg once daily, when needed, can be used. In NSAID treated patients at risk of developing gastric and duodenal ulcers, subsequent symptom control using an on demand regimen is not recommended.
Adults:
In combination with an appropriate antibacterial therapeutic regimen for the eradication of Helicobacter pylori and healing of Helicobacter pylori associated duodenal ulcer and prevention of relapse of peptic ulcers in patients with Helicobacter pylori associated ulcers 20 mg Esolinda with 1 g amoxicillin and 500 mg clarithromycin, all twice daily for 7 days.
Patients requiring continued NSAID therapy
Healing of gastric ulcers associated with NSAID therapy: The usual dose is 20 mg once daily. The treatment duration is 4-8 weeks.
Prevention of gastric and duodenal ulcers associated with NSAID therapy in patients at risk: 20 mg once daily.
Treatment of Zollinger-Ellison Syndrome - The recommended initial dosage is Esolinda 40 mg twice daily. The dosage should then be individually adjusted and treatment continues as long as clinically indicated. Based on the clinical data available, the majority of patients can be controlled on doses between 80 to 160 mg esomeprazole daily. With doses above 80 mg daily, the dose should be divided and given twice-daily.
Adolescents from the age of 12 years - Treatment of duodenal ulcer caused by Helicobacter pylori:
When selecting appropriate combination therapy, consideration should be given to official national, regional and local guidance regarding bacterial resistance, duration of treatment (most commonly 7 days but sometimes up to 14 days), and appropriate use of antibacterial agents. The treatment should be supervised by a specialist.
The posology recommendation is: Weight 30 - 40 kg - combination with two antibiotics: Esolinda 20 mg, amoxicillin 750 mg and clarithromycin 7.5 mg/kg body weight are all administered together twice daily for one week. Weight > 40 kg - combination with two antibiotics: Esolinda 20 mg, amoxicillin 1 g and clarithromycin 500 mg are all administered together twice daily for one week.
Impaired renal function - Dose adjustment is not required in patients with impaired renal function.
Impaired hepatic function - Dose adjustment is not required in patients with mild to moderate liver impairment. For patients with severe liver impairment, a maximum dose of 20 mg Esolinda should not be exceeded.
Elderly - Dose adjustment is not required in the elderly.
Side-effects:
Blood and lymphatic system disorders: Rare: Leukopenia, thrombocytopenia, Very rare: Agranulocytosis, pancytopenia
Immune system disorders. Rare: Hypersensitivity reactions e.g. fever, angioedema and anaphylactic reaction/shock.
Metabolism and nutrition disorders: Uncommon: Peripheral oedema. Rare: Hyponatraemia. Not known: Hypomagnesaemia; severe hypomagnesaemia can correlate with hypocalcaemia.
Psychiatric disorders: Uncommon: Insomnia. Rare: Agitation, confusion, depression. Very rare: Aggression, hallucinations.
Nervous system disorders: Common: Headache. Uncommon: Dizziness, paraesthesia, somnolence. Rare: Taste disturbance
Eye disorders: Rare: Blurred vision.
Ear and labyrinth disorders: Uncommon: Vertigo
Respiratory, thoracic and mediastinal disorders: Rare: Bronchospasm,
Gastrointestinal disorders: Common: Abdominal pain, constipation, diarrhoea, flatulence, nausea/vomiting. Uncommon: Dry mouth. Rare: Stomatitis, gastrointestinal candidiasis. Not known: Microscopic colitis.
Hepatobiliary disorders: Uncommon: Increased liver enzymes. Rare: Hepatitis with or without jaundice. Very rare: Hepatic failure, encephalopathy in patients with pre-existing liver disease.
Skin and subcutaneous tissue disorders: Uncommon: Dermatitis, pruritus, rash, urticaria. Rare: Alopecia, photosensitivity. Very rare: Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN).
Musculoskeletal and connective tissue disorders: Uncommon: Fracture of the hip, wrist or spine. Rare: Arthralgia, myalgia. Very rare: Muscular weakness
Renal and urinary disorders: Very rare: Interstitial nephritis; in some patients renal failure has been reported concomitantly.
Reproductive system and breast disorders: Very rare: Gynaecomastia.
General disorders and administration site conditions: Rare: Malaise, increased sweating.
Overdose:
There is very limited experience to date with deliberate overdose. The symptoms described in connection with 280 mg were gastrointestinal symptoms and weakness. Single doses of 80 mg esomeprazole were uneventful.
Treatment: No specific antidote is known. Esomeprazole is extensively plasma protein bound and is therefore not readily dialyzable. As in any case of overdose, treatment should be symptomatic and general supportive measures should be utilised.
Drug interaction:
Effects of esomeprazole on the pharmacokinetics of other drugs:
Medicinal products with pH dependent absorption Gastric acid suppression during treatment with esomeprazole and other PPIs might decrease or increase the absorption of medicinal products with a gastric pH dependent absorption. As with other medicinal products that decrease intragastric acidity, the absorption of medicinal products such as ketoconazole, itraconazole and erlotinib can decrease and the absorption of digoxin can increase during treatment with esomeprazole.
Omeprazole has been reported to interact with some protease inhibitors. The clinical importance and the mechanisms behind these reported interactions are not always known. Increased gastric pH during omeprazole treatment may change the absorption of the protease inhibitors. Other possible interaction mechanisms are via inhibition of CYP2C19. For atazanavir and nelfinavir, decreased serum levels have been reported when given together with omeprazole and concomitant administration is not recommended.
Treatment with omeprazole 20 mg qd had no effect on the exposure of darunavir (with concomitant ritonavir) and amprenavir (with concomitant ritonavir). Treatment with esomeprazole 20 mg qd had no effect on the exposure of amprenavir (with and without concomitant ritonavir). Treatment with omeprazole 40 mg qd had no effect on the exposure of lopinavir (with concomitant ritonavir). Due to the similar pharmacodynamic effects and pharmacokinetic properties of omeprazole and esomeprazole, concomitant administration with esomeprazole and atazanavir is not recommended and concomitant administration with esomeprazole and nelfinavir is contraindicated.
Drugs metabolised by CYP2C19:
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. This should be considered especially when prescribing esomeprazole for on-demand therapy.
Monitoring is recommended when initiating and ending concomitant esomeprazole treatment during treatment with warfarin or other coumarin derivatives.
Esomeprazole has been shown to have no clinically relevant effects on the pharmacokinetics of amoxicillin or quinidine.
Studies evaluating concomitant administration of esomeprazole and either naproxen or rofecoxib did not identify any clinically relevant pharmacokinetic interactions during short-term studies.
Inconsistent data on the clinical implications of a PK/PD interaction of esomeprazole in terms of major cardiovascular events have been reported from both observational and clinical studies. As a precaution concomitant use of clopidogrel should be discouraged.
Unknown mechanism
Concomitant administration of esomeprazole has been reported to increase the serum levels of tacrolimus.
When given together with PPIs, methotrexate levels have been reported to increase in some patients. In high-dose methotrexate administration a temporary withdrawal of esomeprazole may need to be considered.
Effects of other drugs on the pharmacokinetics of esomeprazole:
Esomeprazole is metabolised by CYP2C19 and CYP3A4. Concomitant administration of esomeprazole and a CYP3A4 inhibitor, clarithromycin (500 mg b.i.d.), resulted in a doubling of the exposure (AUC) to esomeprazole. Concomitant administration of esomeprazole and a combined inhibitor of CYP2C19 and CYP3A4 may result in more than doubling of the esomeprazole exposure. The CYP2C19 and CYP3A4 inhibitor voriconazole increased omeprazole AUCτ by 280%. A dose adjustment of esomeprazole is not regularly required in either of these situations. However, dose adjustment should be considered in patients with severe hepatic impairment and if long-term treatment is indicated.
Drugs known to induce CYP2C19 or CYP3A4 or both (such as rifampicin and St. John's wort) may lead to decreased esomeprazole serum levels by increasing the esomeprazole metabolism.
Cautions:
In the presence of any alarm symptom (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 Esolinda 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.
When prescribing esomeprazole for eradication of Helicobacter pylori, possible drug interactions for all components in the triple therapy should be considered. Clarithromycin is a potent inhibitor of CYP3A4 and hence contraindications and interactions for clarithromycin should be considered when the triple therapy is used in patients concurrently taking other drugs metabolised via CYP3A4 such as cisapride.
Treatment with proton pump inhibitors may lead to slightly increased risk of gastrointestinal infections such as Salmonella and Campylobacter.
Esomeprazole, as all acid-blocking medicines, may reduce the absorption of vitamin B12 (cyanocobalamin) due to hypo- or achlorhydria. This should be considered in patients with reduced body stores or risk factors for reduced vitamin B12 absorption on long-term therapy.
Esomeprazole is a CYP2C19 inhibitor. When starting or ending treatment with esomeprazole, the potential for interactions with drugs metabolised through CYP2C19 should be considered. An interaction is observed between clopidogrel and esomeprazole . The clinical relevance of this interaction is uncertain. As a precaution, concomitant use of esomeprazole and clopidogrel should be discouraged.
Severe hypomagnesaemia has been reported in patients treated with proton pump inhibitors (PPIs) like esomeprazole for at least three months, and in most cases for a year. Serious manifestations of hypomagnesaemia such as fatigue, tetany, delirium, convulsions, dizziness and ventricular arrhythmia can occur but they may begin insidiously and be overlooked. In most affected patients, hypomagnesaemia improved after magnesium replacement and discontinuation of the PPI.
For patients expected to be on prolonged treatment or who take PPIs with digoxin or drugs that may cause hypomagnesaemia (e.g. diuretics), healthcare professionals should consider measuring magnesium levels before starting PPI treatment and periodically during treatment.
Proton pump inhibitors, especially if used in high doses and over long durations (>1 year), may modestly increase the risk of hip, wrist and spine fracture, predominantly in the elderly or in presence of other recognised risk factors. Patients at risk of osteoporosis should receive care according to current clinical guidelines and they should have an adequate intake of vitamin D and calcium.
Increased Chromogranin A (CgA) level may interfere with investigations for neuroendocrine tumours. To avoid this interference, esomeprazole treatment should be stopped for at least 5 days before CgA measurements.
Effects on ability to drive and use machines:
Has no influence on the ability to drive and use machines.
Presentation:
Esolinda 20 or 40 mg: 2x10, alu-alu blister in a carton box with instruction for use.
Storage:
Keep in dry place, protected from light at a temperature below 30°C. Keep out of reach of children.
Shelf life:
Labeled. Do not use after expiry date.
Distribution Condition:
Prescribed medicine.

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BELINDA

Manufactured for:
Branch of Apteki 36.6 Ltd.
Kabul, Afghanistan
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