Exazole®

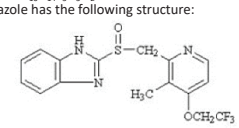
(Lansoprazole 30mg Tablet)

ایکسازول

(لینسوپرازول ۳۰ ملی گرام ٹیبلٹ)

COMPOSITION
Each enteric coated tablet contains:
Lansoprazole BP 30mg

DESCRIPTION
Lansoprazole, a substituted Benzimidazole, 2-[[[3-Methyl-4- (2,2, 2-Trifluoroethoxy)-2-Pyridyl] Methyl] Sulfinyl] Benzimidazole, a compound that inhibits gastric acid secretion. Its empirical formula is $C_{16}H_{14}F_3N_3O_2S$ with a molecular weight of 369.37. Lansoprazole has the following structure:



CLINICAL PHARMACOLOGY
Mechanism of Action
Lansoprazole belongs to a class of antisecretory compounds, the substituted Benzimidazoles, that suppress gastric acid secretion by specific inhibition of the (H+, K+)-ATPase enzyme system at the secretory surface of the gastric parietal cell. Because this enzyme system is regarded as the acid (Proton pump) within the parietal cell, Lansoprazole has been characterized as a gastric acid-pump inhibitor, in that it blocks the final step of acid production. Lansoprazole inhibited the normal increases in secretion volume, acidity and acid output induced by insulin.

Pharmacodynamics
Antisecretory Activity
After oral administration, Lansoprazole was shown to significantly decrease the basal acid output and significantly increase the mean gastric pH and percent of time the gastric pH was greater than three and greater than four. Lansoprazole also significantly reduced meal-stimulated gastric acid output and secretion volume, as well as pentagastrin-stimulated acid output.

Pharmacokinetics
Absorption: The absorption of Lansoprazole is rapid, with the mean Cmax occurring approximately 1.7 hours after oral dosing, and the absolute bioavailability is over 80%. In healthy subjects, the mean (±SD) plasma half-life was 1.5 (±1.0) hours. Both the Cmax and AUC are diminished by about 50% to 70% if Lansoprazole is given 30 minutes after food, compared to the fasting condition. There is no significant food effect if Lansoprazole is given before meals.

Distribution: Lansoprazole is 97% bound to plasma proteins. Plasma protein binding is constant over the concentration range of 0.05 to 5.0 mcg/mL.

Metabolism: Lansoprazole is extensively metabolized in the liver. Two metabolites have been identified in measurable quantities in plasma (the Hydroxylated Sulfinyl and Sulfone derivatives of Lansoprazole). These metabolites have very little or no antisecretory activity. Lansoprazole is thought to be transformed into two active species which inhibit acid secretion by blocking the proton pump [(H+ , K+)-ATPase enzyme system] at the secretory surface of the gastric parietal cell. The two active species are not present in the systemic circulation. The plasma elimination half-life of Lansoprazole is less than 2 hours while the acid inhibitory effect lasts more than 24 hours. Therefore, the plasma elimination half-life of Lansoprazole does not reflect its duration of suppression of gastric acid secretion.

Elimination: Following single-dose oral administration of Lansoprazole, virtually no unchanged Lansoprazole was excreted in the urine. In one study, after a single oral dose of ^{14}C-Lansoprazole, approximately one-third of the administered radiation was excreted in the urine and two-thirds was recovered in the feces. This implies a significant biliary excretion of the Lansoprazole metabolites.

INDICATIONS
Short-Term Treatment of Active Duodenal Ulcer: Lansoprazole is indicated for short-term treatment (for 4 weeks) for healing and symptom relief of active duodenal ulcer.

H.Pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence Triple Therapy: Lansoprazole in combination with Amoxicillin plus Clarithromycin as triple therapy is indicated for the treatment of patients with H.Pylori infection and duodenal ulcer disease (active or one-year history of a duodenal ulcer) to eradicate H.Pylori.

Dual Therapy: Lansoprazole in combination with Amoxicillin as dual therapy is indicated for the treatment of patients with H.Pylori infection and duodenal ulcer disease (active or one-year history of a duodenal ulcer).

Maintenance of Healed Duodenal Ulcers: Lansoprazole is indicated to maintain healing of duodenal ulcers. Controlled studies do not extend beyond 12 months.

Short-Term Treatment of Active Benign Gastric Ulcer: Lansoprazole is indicated for short-term treatment (up to 8 weeks) for healing and symptom relief of active benign gastric ulcer.

Healing of NSAID-Associated Gastric Ulcer Lansoprazole is indicated for the treatment of NSAID-associated gastric ulcer in patients who continue NSAID use. Controlled studies did not extend beyond 8 weeks Risk Reduction of NSAID-Associated.

Risk Reduction of NSAID-Associated Gastric Ulcer: Lansoprazole is indicated for reducing the risk of NSAID-associated gastric ulcers in patients with a history of a documented gastric ulcer who require the use of an NSAID. Controlled studies did not extend beyond 12 weeks.

Gastroesophageal Reflux Disease (GERD) Short-Term Treatment of Symptomatic GERD: Lansoprazole is indicated for the treatment of heartburn and other symptoms associated with GERD.

Short-Term Treatment of Erosive Esophagitis: Lansoprazole is indicated for short-term treatment (up to 8 weeks) for healing and symptom relief of all grades of erosive Esophagitis. For patients who do not heal with Lansoprazole for 8 weeks (5 to 10%), it may be helpful to give an additional 8 weeks of treatment. If there is a recurrence of erosive Esophagitis an additional 8-week course of Lansoprazole may be considered.

Maintenance of Healing of Erosive Esophagitis (EE): Lansoprazole is indicated to maintain healing of erosive Esophagitis. Controlled studies did not extend beyond 12 months.

Pathological Hypersecretory Conditions Including: Lansoprazole is indicated for the long-term treatment of Pathological hypersecretory conditions, including Zollinger-Ellison syndrome.

DOSAGE AND ADMINISTRATION
Recommended Dose

INDICATION	RECOMMENDED DOSE	FREQUENCY
Duodenal Ulcers		
Short-Term Treatment	15mg	Once daily for 4 weeks
Maintenance of Healed	15mg	Once daily
H.Pylori Eradication to Reduce the Risk of Duodenal		
Ulcer Recurrence*		
Triple Therapy:		
Lansoprazole	30mg	Twice daily (q12h) for 10 or 14 days
Amoxicillin	1gram	Twice daily (q12h) for 10 or 14 days
Clarithromycin	500mg	Twice daily (q12h) for 10 or 14 days
Dual Therapy:		
Lansoprazole	30mg	Three times daily (q8h) for 14 days
Amoxicillin	1gram	Three times daily (q8h) for 14 days
Benign Gastric Ulcer		
Short-Term Treatment	30mg	Once daily for up to 8 weeks
NSAID-associated Gastric Ulcer		
Healing	30mg	Once daily for 8 weeks†
Risk Reduction	15mg	Once daily for up to 12 weeks†
Gastroesophageal Reflux Disease (GERD)		
Short-Term Treatment of Symptomatic GERD	15 mg	Once daily for up to 8 weeks
Short-Term Treatment of Erosive Esophagitis	30 mg	Once daily for up to 8 weeks‡
Pediatric		
(1 to 11 years of age) Short-Term Treatment of Symptomatic GERD and Short-Term Treatment of Erosive Esophagitis		
≥ 30 kg	15mg	Once daily for up to 12 weeks
> 30 kg	30mg	Once daily for up to 12 weeks
(12 to 17 years of age) Short-Term Treatment of Symptomatic GERD		
Nonerosive GERD	15mg	Once daily for up to 8 weeks
Erosive Esophagitis	30mg	Once daily for up to 8 weeks
Maintenance of Healing of Erosive Esophagitis	15mg	Once daily
Pathological Hypersecretory Conditions Including Zollinger-Ellison Syndrome	60mg	Once daily

† Controlled studies did not extend beyond indicated duration.

† For patients who do not heal with Lansoprazole for eight weeks (5 to 10%), it may be helpful to give an additional eight weeks of treatment. If there is a recurrence of erosive Esophagitis, an additional eight week course of Lansoprazole may be considered.

The Lansoprazole dose was increased (up to 30 mg twice daily) in some pediatric patients after two or more weeks of treatment if they remained symptomatic. For pediatric patients unable to swallow an intact capsule please see Administration Options.
Controlled studies did not extend beyond 12 months

Varies with individual patient. Recommended adult starting dose is 60 mg once daily. Doses should be adjusted to individual patient needs and should continue for as long as clinically indicated. Dosages up to 90 mg twice daily have been administered. Daily dose of greater than 120 mg should be administered in divided doses. Some patients with Zollinger-Ellison Syndrome have been treated continuously with Lansoprazole for more than four years.

CONTRAINDICATIONS
Lansoprazole is contraindicated in patients with known severe hypersensitivity to any component of the formulation of Lansoprazole. Hypersensitivity reactions may include Anaphylaxis, Anaphylactic shock, Angioedema, Bronchospasm, acute interstitial Nephritis, and Urticaria.

WARNING AND PRECAUTIONS
Gastric Malignancy
Symptomatic response to therapy with Lansoprazole does not preclude the presence of Gastric Malignancy.

Acute Interstitial Nephritis
Acute interstitial Nephritis has been observed in patients taking PPIs including Lansoprazole. Acute interstitial Nephritis may occur at any point during PPI therapy and is generally attributed to an idiopathic hypersensitivity reaction. Discontinue Lansoprazole if acute interstitial Nephritis develops.

Cyanocobalamin (Vitamin B12) Deficiency
Daily treatment with any acid-suppressing medications over a long period of time (e.g., longer than 3 years) may lead to malabsorption of Cyanocobalamin (Vitamin B12) caused by hypo- or Achlorhydria.

Clostridium Difficile Associated Diarrhea
Published observational studies suggest that proton pump inhibitor (PPI) therapy like Lansoprazole may be associated with an increased risk of Clostridium difficile associated diarrhea (CDAD), especially in hospitalized patients.

Bone Fracture
Several published observational studies suggest that PPI therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist or spine.

Hypomagnesemia
Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPIs for at least three months, in most cases after a year of therapy.

ADVERSE REACTIONS
Body as a Whole: Anaphylactic/Anaphylactoid reactions
Digestive System: Hepatotoxicity, Pancreatitis, Vomiting
Hemic and Lymphatic System: Agranulocytosis, Aplastic Anemia, Hemolytic Anemia, Leukopenia, Neutropenia, Pancytopenia, Thrombocytopenia, and Thrombotic Thrombocytopenic purpura
Infections and Infestations: Clostridium difficile associated diarrhea
Metabolism and Nutritional Disorders: Hypomagnesemia;
Musculoskeletal System: Bone fracture, Myositis
Skin and Appendages: Severe dermatologic reactions including Erythema multiforme, Stevens Johnson syndrome, toxic epidermal Necrolysis (some fatal)
Special Senses: Speech disorder
Urogenital System: Interstitial Nephritis, urinary retention

DRUG INTERACTIONS
Drugs with pH-Dependent Absorption Kinetics Lansoprazole causes Long-lasting Inhibition Of Gastric Acid Secretion. Lansoprazole and other PPIs are likely to substantially decrease the systemic concentrations of the HIV protease inhibitor Atazanavir, which is dependent upon the presence of gastric acid for absorption, and may result in a loss of therapeutic effect of Atazanavir and the development of HIV resistance. Therefore, Lansoprazole and other PPIs should not be Co-administered with Atazanavir. Lansoprazole and other PPIs may interfere with the absorption of other drugs where gastric pH is an important determinant of oral bioavailability (e.g., Ampicillin Esters, Digoxin, Iron salts, Ketoconazole)

Warfarin
In a study of healthy subjects, Co-Administration of single or multiple 60mg doses of Lansoprazole and warfarin did not affect the Pharmacokinetics of warfarin nor Prothrombin time. However, there have been reports of increased INR and Prothrombin time in patients receiving PPIs and warfarin concomitantly. Increases in INR and Prothrombin time may lead to abnormal bleeding and even death. Patients treated with PPIs and warfarin concomitantly may need to be monitored for increases in INR and Prothrombin time.

Tacrolimus
Concomitant administration of Lansoprazole and Tacrolimus may increase whole blood levels of Tacrolimus, especially in transplant patients who are intermediate or poor metabolizers of CYP2C19.

Theophylline
A minor increase (10%) in the clearance of Theophylline was observed following the administration of Lansoprazole concomitantly with Theophylline. Although the magnitude of the effect on Theophylline clearance is small, individual patients may require additional titration of their Theophylline dosage when Lansoprazole is started or stopped to ensure clinically effective blood levels

Clopidogrel
Concomitant administration of Lansoprazole and Clopidogrel in healthy subjects had no clinically important effect on exposure to the active metabolite of Clopidogrel or Clopidogrel-induced platelet inhibition. No dose adjustment of Clopidogrel is necessary when administered with an approved dose of Lansoprazole.

Methotrexate
Case reports, published population Pharmacokinetic studies, and retrospective analyses suggest that concomitant administration of PPIs and Methotrexate may elevate and prolong serum levels of Methotrexate and/or its metabolite Hydroxymethotrexate. However, no formal drug interaction studies of high dose Methotrexate with PPIs have been conducted In a study of Rheumatoid arthritis patients receiving low-dose Methotrexate, Lansoprazole and naproxen, no effect on Pharmacokinetics of Methotrexate was observed

Combination Therapy with Clarithromycin
Concomitant administration of Clarithromycin with other drugs can lead to serious adverse reactions due to drug interactions. Because of these drug interactions, Clarithromycin is contraindicated for Co-Administration with certain drugs

OVERDOSAGE
Lansoprazole is not removed from the circulation by Hemodialysis. In one reported overdose, a patient consumed 600mg of Lansoprazole with no adverse reaction. Oral Lansoprazole doses up to 5000mg/kg in rats [approximately 1300 times the 30mg human dose based on body surface area (BSA)] and in mice (about 675.7 times the 30mg human dose based on BSA) did not produce deaths or any clinical signs.

STORAGE:
Store below 30°C.
Tablet should be swallowed whole, not chewed.
Protect from heat, light and moisture.
Keep out of the reach of children.

PRESENTATION:
Exazole (Lansoprazole) 30mg Tablet:
Pack of 14 's in Alu-Alu blister.

(R002)

خوراک اور ہدایات:

ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
دوا کو **30** درجہ سینٹی گریڈ سے کم درجہ حرارت پر رکھیں۔
گولی کو چبائے بغیر پانی سے نگل لیں۔
روشنی ، گرمی اور نمی سے بچائیں۔
بچوں کی پہنچ سے دور رکھیں۔

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