Nexprazole®
(E s o m e p r a z o l e)

نیکسپرازول

QUALITATIVE AND QUANTITATIVE COMPOSITION
Nexprazole Capsule 20mg
Each capsule contains:
Esomeprazole Magnesium trihydrate (Enteric-coated pellets) equivalent to Esomeprazole. .... 20 mg
Nexprazole Capsule 40mg
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Esomeprazole Magnesium trihydrate (Enteric-coated pellets) equivalent to Esomeprazole. .... 40 mg

DESCRIPTION
The active ingredient in the proton pump inhibitor Nexprazole is esomeprazole magnesium. Chemically, it is bis (5-methoxy-2[(S)-[(4-methoxy-3, 5-dimethyl -2-pyridinyl) methyl]sulfinyl] -1*H*-benzimidazole-1-yl) magnesium trihydrate. Esomeprazole is the S-isomer of omeprazole, which is a mixture of the S-and R-isomers. Its molecular formula is $(C_{17}H_{18}N_3O_3S)_2Mg \times 3\ H_2O$ with molecular weight of 767.2 as a trihydrate and 713.1 on an anhydrous basis.

CLINICAL INFORMATION
Indications
Nexprazole (Esomeprazole) is indicated for:
1. *Gastroesophageal Reflux Disease (GERD)*
- Healing of erosive esophagitis
- Maintenance of healing of erosive esophagitis.
- Symptomatic gastro esophageal reflux disease (GERD).

2. *Risk Reduction of NSAID Associated Gastric Ulcer*
3. *H. pylori Eradication to Reduce the Risk of Duodenal Ulcer Recurrence*
- Triple Therapy (Nexprazole plus amoxicillin and clarithromycin):

Nexprazole (Esomeprazole), in combination with amoxicillin and clarithromycin, is indicated for the treatment of patients with H. pylori infection and duodenal ulcer disease (active or history of within the past 5 years) to eradicate H. pylori. Eradication of H. pylori has been shown to reduce the risk of duodenal ulcer recurrence.
4. *Pathological Hypersecretory Conditions Including Zollinger-Ellison Syndrome*

Dosage and Administration
The recommended adult dosages are outlined in the table below. Nexprazole (Esomeprazole) capsules should be swallowed whole and taken at least one hour before meals.

Recommended Adult Dosage Schedule		
Indication	**Dose**	**Frequency**
I. Gastroesophageal Reflux Disease		
Healing of erosive esophagitis	20 mg or 40 mg	Once daily 4 to 8 weeks
Maintenance of healing erosive esophagitis	20 mg	Once daily
Symptomatic gastroesophageal reflux disease	20mg	Once daily for 4 weeks
Pediatric GERD		
12 to 17 year old		
Healing of Erosive Esophagitis	20 mg or 40 mg	Once Daily for 4 to 8 weeks
Symptomatic GERD	20	Once daily up to 4weeks
1 to 11 Year Old		
Short-term Treatment of Symptomatic GERD	10 mg	Once Daily for up to 8 Weeks
Healing of Erosive Esophagitis		
weight < 20 kg	10 mg	Once Daily for 8 Weeks
weight ≥ 20 kg	10 mg or 20 mg	Once Daily for 8 Weeks
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 Nexprazole Amoxicillin Clarithromycin	 40 mg 1000 mg 500 mg	 Once daily for 10 days Twice daily for 10 days Twice daily for 10 days
IV. Pathological Hypersecretory Condiions including Zollinger-Ellison Syndrome	40 mg	Twice daily

Heading as Dosage Adjustment
Hepatic Insufficiency
In patients with mild to moderate liver impairment (Child-Pugh Classes A and B), no dosage adjustment is necessary. For patients with severe liver impairment (Child-Pugh Class C), a dose of 20 mg of Nexprazole (Esomeprazole) should not be exceeding.
Administration requirements
Let patients know that antacids may be used while taking Nexprasole (Esomeprazole).
Advise patients to take Nexprazole (Esomeprazole) at least one hour before a meal.

Contraindications
Esomeprazole is contraindicated in patients with known hypersensitivity to substituted benzimidazoles or to any component of the formulation.

Warnings and precautions
Presence of Gastric Malignancy
In adults, symptomatic response to therapy with esomeprazole does not preclude the presence of gastric malignancy. Consider additional follow-up and diagnostic testing in adult patients who have a suboptimal response or an early symptomatic relapse after completing treatment with a PPI. In older patients, also consider an endoscopy.
Acute Interstitial Nephritis
Acute interstitial nephritis may occur at any point during PPI therapy and is generally attributed to an idiopathic hypersensitivity reaction. Discontinue Nexprazole (Esomeprazole) if acute interstitial nephritis develops.
Clostridium difficile-Associated Diarrhea
PPI therapy like esomeprazole may be associated with an increased risk of *Clostridium difficile*-associated diarrhea, especially in hospitalized patients. This diagnosis should be considered for diarrhea that does not improve. Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.
Bone Fracture
Proton pump inhibitor (PPI) therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine. The risk of fracture was increased in patients who received high-dose, defined as multiple daily doses, and long-term PPI therapy (a year or longer). Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.
Cutaneous and Systemic Lupus Erythematosus
Cutaneous lupus erythematosus (CLE) and systemic lupus erythematosus (SLE) have been reported in patients taking PPIs, including esomeprazole. Avoid administration of PPIs for longer than medically indicated. If signs or symptoms consistent with CLE or SLE are noted in patients receiving Esomeprazole, discontinue the drug.
Cyanocobalamin (Vitamin B-12) 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 B-12) caused by hypo-or achlorhydria.. This diagnosis should be considered if clinical symptoms consistent with cyanocobalamin deficiency are observed.
Hypomagnesemia
Hypomagnesemia, symptomatic and asymptomatic, is known to occur rarely in patients treated with PPIs for at least three months, in most cases after a year of therapy.
Interaction with St. John's Wort or Rifampin
Drugs which induce CYP2C19 or CYP3A4 (such as St. John's Wort or rifampin) can substantially decrease esomeprazole concentrations. Avoid concomitant use of Esomeprazole with St. John's Wort or rifampin.
Interaction with Clopidogrel
Avoid concomitant use of Esomeprazole with clopidogrel.
Interactions with Diagnostic Investigations for Neuroendocrine Tumors
Serum chromogranin A (CgA) levels increase secondary to drug-induced decreases in gastric acidity.Healthcare providers should temporarily stop esomeprazole treatment at least 14 days before assessing CgA levels and consider repeating the test if initial CgA levels are high.
Interaction with Methotrexate
Concomitant use of PPIs with methotrexate (primarily at high dose; see methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or its metabolite, possibly leading to methotrexate toxicities.
Pregnancy & Lactation
There is insufficient data available in pregnant women. Esomeprazole should be used during pregnancy only if clearly needed. Because esomeprazole is likely to be excreted in human milk a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account importance of the drug to the mother due to the potential for serious adverse reactions nursing infants from esomeprazole.
Fundic Gland Polyps
PPI use is associated with an increased risk of fundic gland polyps that

increases with long-term use, especially beyond one year. Most PPI users who developed fundic gland polyps were asymptomatic and fundic gland polyps were identified incidentally on endoscopy. Use the shortest duration of PPI therapy appropriate to the condition being treated.

Interactions

Interference with Antiretroviral Therapy

Concomitant use of atazanavir and nelfinavir with proton pump inhibitors is not recommended. 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.

Drugs for Which Gastric pH Can Affect Bioavailability

Due to its effects on gastric acid secretion, esomeprazole can reduce the absorption of drugs where gastric pH is an important determinant of their bioavailability. Like with other drugs that decrease the intragastric acidity, the absorption of drugs such as ketoconazole, atazanavir, iron salts, erlotinib, and mycophenolate mofetil (MMF) can decrease, while the absorption of drugs such as digoxin can increase during treatment with esomeprazole.

Effects on Hepatic Metabolism/Cytochrome P-450 Pathways

Esomeprazole is extensively metabolized in the liver by CYP2C19 and CYP3A4. *E*someprazole is not likely to inhibit CYPs 1A2, 2A6, 2C9, 2D6, 2E1, and 3A4. No clinically relevant interactions with drugs metabolized by these CYP enzymes would be expected. It is known that esomeprazole does not have any clinically significant interactions with phenytoin, warfarin, quinidine, clarithromycin, or amoxicillin. 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. Co-administration of esomeprazole 30 mg and diazepam, a CYP2C19 substrate, resulted in a 45% decrease in clearance of diazepam.

Clopidogrel

Clopidogrel is metabolized to its active metabolite in part by CYP2C19. Concomitant use of esomeprazole 40 mg results in reduced plasma concentrations of the active metabolite of clopidogrel and a reduction in platelet inhibition. Avoid concomitant administration of esomeprazole with clopidogrel.

Omeprazole acts as an inhibitor of CYP2C19. Omeprazole, given in doses of 40 mg daily for one week to 20 healthy subjects in cross-over study, increased C_{max} and AUC of cilostazol by 18% and 26% respectively. C_{max} and AUC of one of its active metabolites, 3, 4-dihydrocilostazol, which has 4-7 times the activity of cilostazol, were increased by 29% and 69%, respectively. Co-administration of cilostazol with esomeprazole is expected to increase concentrations of cilostazol and its above mentioned active metabolite. Therefore, a dose reduction of cilostazol from 100 mg twice daily to 50 mg twice daily should be considered.

Concomitant administration of esomeprazole and a combined inhibitor of CYP2C19 and CYP3A4, such as voriconazole, may result in more than doubling of the esomeprazole exposure. Dose adjustment of esomeprazole is not normally required. However, in patients with Zollinger-Ellison's Syndrome, who may require higher doses up to 240 mg/day, dose adjustment may be considered.

Drugs known to induce CYP2C19 or CYP3A4 or both (such as rifampin) may lead to decreased esomeprazole serum levels. esomeprazole has been reported to interact with St. John's Wort, an inducer of CYP3A4. Avoid concomitant use of St. John's Wort or rifampin with esomeprazole.

Interactions with Investigations of Neuroendocrine Tumors

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.

Tacrolimus

Concomitant administration of esomeprazole and tacrolimus may increase the serum levels of tacrolimus.

Combination Therapy with Clarithromycin

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

Methotrexate

Concomitant administration of PPIs and methotrexate (primarily at high dose; see methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or its metabolite hydroxymethotrexate.

Pregnancy and Breastfeeding

Pregnancy Category B

There are no adequate and well-controlled studies with esomeprazole in pregnant women. Available epidemiologic data fail to demonstrate an increased risk of major congenital malformations or other adverse pregnancy outcomes with first trimester omeprazole use.

There are no clinical data on the effects of esomeprazole on the breastfed infant or on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for esomeprazole and any potential adverse effects on the breastfed infant.

Effects on ability to drive and use machines

Esomeprazole has minor influence on the ability to drive and use machines. Adverse reactions such as dizziness (uncommon) and blurred vision (rare) are known to occur. If affected patients should not drive or use machines.

Adverse Reactions

The reactions are classified according to frequency very common ≥1/10; common ≥1/100 to <1/10.

System Organ Class	Frequency	Undesirable Effect
Nervous system disorders	Common	Headache
	Uncommon	Dizziness, paraesthesia, somnolence
Gastrointestinal disorders	Common	Abdominal pain, constipation, diarrhoea, flatulence, nausea/vomiting, fundic gland polyps (benign)
	Uncommon	Dry mouth
Metabolism and nutrition disorders	Uncommon	Peripheral oedema
Psychiatric disorders	Uncommon	Insomia
Ear and labyrinth disorders	Uncommon	Vertigo
Hepatobiliary disorders	Uncommon	Increased liver enzymes
Skin and subcutaneous tissue disorders	Uncommon	Dermatitis, pruritus, rash, urticaria
Musculoskeletal and connective tissue disorders	Uncommon	Fracture of the hip, wrist or spine

Overdose

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.

PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: Drugs for acid-related disorders proton pump inhibitors

ATC code: A02B C05

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 20 to 40 mg and leads to inhibition of gastric acid secretion.

Pharmacokinetics properties

Absorption

The AUC after administration of a single 40 mg dose of esomeprazole is decreased by 43% to 53% after food intake compared to fasting conditions. esomeprazole should be taken at least one hour before meals.

Distribution

Nexprazole (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 CYP2C19 isoenzyme, which forms the hydroxy and desmethyl metabolites.

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.

PHARMACEUTICAL INFORMATION
Shelf life
2 years

Special Precautions for Storage
To be sold on the prescription of a registered medical practitioner only.
Protect from light and moisture.
Do not store above 30°C.
Keep out of the reach of children.

ہدایات:
صرف مستند ڈاکٹر کے نسخے پر فروخت کریں۔
۳۰ ڈگری سینٹی گریڈ سے زیادہ درجہ حرارت پر نہ رکھیں۔
دوا کو روشنی اور نمی سے محفوظ رکھیں۔ بچوں کی پہنچ سے دور رکھیں۔

Nature and contents of container
Nexprazole (Esomeprazole) 20mg capsules are available in the blister pack of 14's (2x7's).
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MANUFACTURED BY

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