ESONEXT® 20 & 40

(USP Specification)

Esomeprazole

(Manufacturer Specification)

20mg & **40**mg Capsules

COMPOSITION

ESONEXT 20mg Capsules: Each capsule contains:
Enteric coated pellets of Esomeprazole Magnesium Trihydrate eq. to Esomeprazole ..... 20mg.
(USP Specification)

ESONEXT 40mg Capsules: Each capsule contains:
Enteric coated pellets of Esomeprazole Magnesium Trihydrate eq. to Esomeprazole ..... 40mg.
(USP Specification)

DESCRIPTION

ESONEXT capsule is an enteric coated pellet formulation of esomeprazole magnesium due to its acid labile nature. **ESONEXT** is intended for oral administration. Esomeprazole is the S-isomer of omeprazole, which inhibits gastric acid secretion more effectively than omeprazole. Chemically it is bis(5-methoxy-2-[(S)-[(4-methoxy-3, 5-dimethyl-2-pyridinyl)methyl]sulfinyl]-1H-benzimidazole-1-yl) magnesium trihydrate. The molecular formula is $(C_{17}H_{18}N_3O_3S)_2 Mg \times 3H_2O$.

CLINICAL PARTICULARS

Therapeutic Indications:

ESONEXT (Esomeprazole) is indicated for:

1. Gastroesophageal Reflux Disease (GERD)
   - Treatment of erosive reflux esophagitis
   - Long term management of patients with healed esophagitis to prevent relapse.
   - Symptomatic treatment of gastroesophageal reflux disease (GERD) without esophagitis.
   - Treatment of heartburn and other symptoms associated with GERD
2. As a triple therapy (Esomeprazole plus amoxicillin and clarithromycin) for the eradication of *Helicobacter pylori*
   - Healing of duodenal ulcer associated with *helicobacter pylori* infection.
   - Prevention of relapse of peptic ulcers in patients with *helicobacter pylori* associated ulcers.

Note: In patients who failed the therapy, susceptibility testing should be done. If resistance to clarithromycin is demonstrated or susceptibility testing is not possible, alternative antimicrobial therapy should be instituted.

3. **ESONEXT** is also indicated for the reduction in the occurrence of gastric ulcers associated with continuous NSAID therapy in patients at risk for developing gastric ulcers.

Dosage and administration:

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

RECOMMENDED DOSAGE SCHEDULE

Indication	Dose	Frequency
Gastroesophageal Reflux Disease (GERD)		
Healing of erosive esophagitis	20 mg or 40 mg	Once daily for 4-8 weeks
Maintenance of healing of erosive esophagitis	20 mg	Once daily
Symptomatic gastroesophageal reflux disease	20 mg	Once daily for 4 weeks*
NSAID associated gastric ulcer		
Risk reduction of NSAID associated gastric ulcer	20 mg or 40 mg	Once daily for up to 6 months
H. pylori eradication to reduce the risk of duodenal ulcer recurrence (Triple Therapy)		
Esomeprazole **(ESONEXT)**	40 mg	Once daily for 10 days
Amoxicillin	1000 mg	Twice daily for 10 days
Clarithromycin	500 mg	Twice daily for 10 days

**If symptoms do not resolve completely after 4 weeks, an additional 4 weeks of treatment may be considered.*

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

Contraindications:

ESONEXT (Esomeprazole) is contraindicated in patients with known hypersensitivity to drug or any component of the formulation or to substituted benzimidazoles.

Precautions:

General: In the presence of any alarming symptoms (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 esomeprazole 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 since the symptomatic response to therapy with esomeprazole does not preclude the 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. Patients undergoing on-demand treatment should be instructed to contact their physician if their symptoms change in character. When prescribing esomeprazole for on-demand therapy, the implications for interactions with other pharmaceuticals, due to fluctuating plasma concentrations of esomeprazole should be considered. When prescribing esomeprazole for eradication of helicobacter pylori infection possible drug interactions for other components in the triple therapy should be considered. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Drug interactions:

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 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.

Pediatric use:

Safety and effectiveness in pediatric patients have not been established.

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 esomeparazole 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 in nursing infants from esomeprazole.

Adverse reactions:

The following adverse drug reactions have been reported during therapy of esomeprazole. None found to be dose-related.

Common: Headache, abdominal pain, diarrhoea, flatulence, nausea/vomiting, constipation.

Uncommon: Dermatitis, pruritus, urticaria, dizziness, dry mouth.

Rare: Hypersensitivity reactions e.g. angioedema, anaphylactic reaction.

The following adverse drug reactions have been observed for the racemate omeprazole and may occur with esomeprazole:

Central and peripheral nervous system: Paraesthesia, somnolence, insomnia, vertigo, reversible mental confusion, agitation, aggression, depression and hallucinations, predominantly in severely ill patients.

Endocrine: Gynaecomastia.

Gastrointestinal: Stomatitis and gastrointestinal candidiasis.
Haematological: Leukopenia, thrombocytopenia, agranulocytosis and pancytopenia.
Hepatic: Increased liver enzymes, encephalopathy in patients with pre-existing severe liver disease; hepatitis with or without jaundice, hepatic failure.
Skin: Rash, photosensitivity, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis, alopecia.
Other: Malaise, hypersensitivity reactions e.g. fever, bronchospasm, interstitial nephritis. Increased sweating, peripheral oedema, blurred vision, taste disturbance and hyponatraemia.

CLINICAL PHARMACOLOGY
Pharmacodynamics:
Esomeprazole works by binding irreversibly to the H+/K+ ATPase in the proton pump. Because the proton pump is the final pathway for secretion of hydrochloric acid by the parietal cells in the stomach, its inhibition dramatically decreases the secretion of hydrochloric acid into the stomach and alters gastric pH.
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 to 40mg. At repeated once-daily dosing with 40mg, the systemic bioavailability is approximately 90% compared to 64% after a single dose of 40mg.
Effect of food: The AUC after administration of a single 40mg 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 clearance 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.
Pediatric: The pharmacokinetics of esomeprazole have not been studied in patients <18 years of age.
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.

STORAGE
Store below 30°C. Protect from light and moisture.

HOW SUPPLIED
ESONEXT 20mg Capsules: Pack of 14 capsules.
ESONEXT 40mg Capsules: Pack of 14 capsules.

TO BE SOLD ON THE PRESCRIPTION OF A REGISTERED MEDICAL PRACTITIONER ONLY.

KEEP ALL MEDICINES OUT OF THE REACH OF CHILDREN.

Lactose & Gluten Free

ایسونیکسٹ

(ایس اومیپرازول)

20 ملی گرام اور 40 ملی گرام

کیپسولز

خوراک وہدایات

ڈاکٹر کی ہدایات کے مطابق استعمال کریں۔

صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت کی جائے۔

تمام ادویات بچوں کی پہنچ سے دور رکھیں۔

دوا کو 30°C سے کم درجہ حرارت پر، نمی اور روشنی سے محفوظ رکھیں۔

NEXT PHARMACEUTICAL
Manufactured by:
NEXT Pharmaceutical Products (Pvt.) Ltd.
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