Nexum™ iv

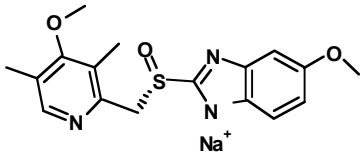
[Esomeprazole]

نیکسم آئی وی

Lyophilized powder for IV injection & Infusion
40mg

DESCRIPTION

The active ingredient in NEXUM IV lyophilized powder for injection is esomeprazole sodium. Its molecular formula is (S)-5-methoxy-2[[(4-methoxy-3, 5-dimethyl-2-pyridinyl)-methyl] sulfinyl]-1 *H*-benzimidazole sodium. Esomeprazole is the S-isomer of omeprazole, which is a mixture of the S- and R-isomers. It inhibits gastric acid secretion more effectively than omeprazole. Its molecular formula is $C_{17}H_{18}N_3O_3SNa$. The structural formula is:



Esomeprazole

QUALITATIVE & QUANTITATIVE COMPOSITION

NEXUM IV (Esomeprazole) is available as:

NEXUM IV 40mg
Each vial contains:
Esomeprazole sodium equivalent to
esomeprazole...40mg
(Suitably buffered)

CLINICAL PHARMACOLOGY

Mechanism of Action

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. By acting specifically on the proton pump, esomeprazole blocks the final step in acid production, thus reducing gastric acidity.

Pharmacokinetics

Distribution

The apparent volume of distribution at steady state in healthy subjects is approximately 0.22L/kg body weight. Esomeprazole is 97% bound to plasma proteins.

Metabolism

Esomeprazole is completely metabolized in the liver 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.

Elimination

Esomeprazole is excreted as metabolites primarily in urine but also in feces. Less than 1% of parent drug is excreted in the urine. Esomeprazole is completely eliminated from plasma and there is no accumulation during once daily administration. The plasma elimination half-life of intravenous esomeprazole is approximately 1.1 to 1.4 hours and is prolonged with increasing dose of intravenous esomeprazole.

Special Populations

Hepatic Insufficiency

The metabolism of esomeprazole in patients with mild to moderate liver dysfunction may be impaired. The metabolic rate is decreased in patients with severe liver dysfunction resulting in a doubling of the total exposure of esomeprazole. Esomeprazole or its major metabolites do not show any tendency to accumulate with once daily dosing.

Geriatric

In oral studies, the AUC and C_{max} values were slightly higher (25% and 18%, respectively) in the elderly as compared to younger subjects at steady state. Dosage adjustment based on age is not necessary.

Pediatric

The pharmacokinetics of esomeprazole sodium have not been studied in patients <18 years of age.

INDICATIONS

NEXUM IV (Esomeprazole) is indicated for gastric anti-secretory treatment when the oral route is not possible:

- For short term treatment of gastro-esophageal reflux disease in patients with esophagitis and/or severe symptoms of reflux.
- Healing of gastric ulcers associated with NSAID therapy.
- Prevention of gastric and duodenal ulcers associated with NSAID therapy, in patients at risk.

DOSAGE & ADMINISTRATION

Short term treatment of GERD with a history of Erosive Esophagitis

The recommended adults dose is either 20 or 40mg esomeprazole given once daily by intravenous injection (no less than 3 minutes) or intravenous infusion (10 to 30 minutes) upto 10 days.

Healing of gastric ulcers as sociated with NSAID therapy

For healing of gastric ulcers associated with NSAID therapy the usual dose is 20mg once daily.

Prevention of gastric and duodenal ulcers associated with NSAID therapy

For prevention of gastric and duodenal ulcers associated with NSAID therapy, patients at risk should be treated with 20mg once daily.

Hepatic Insufficient Patients:

Dose adjustment is not required in patients with mild to moderate liver impairment. For patients with severe liver impairment, a maximum daily dose of 20mg NEXUM IV (Esomeprazole) should not be exceeded.

Elderly

Dose adjustment is not required in the elderly.

Instructions for use

NEXUM IV (Esomeprazole) for Injection should not be administered concomitantly with any other medications through the same intravenous site and/or tubing. The intravenous line should always be flushed with 0.9% sodium chloride solution for injection, Lactated Ringer's injection or 5% dextrose injection both prior to and after administration of NEXUM IV (Esomeprazole) for injection.

Intravenous Injection (20 or 40mg)

The freeze-dried powder should be reconstituted with 5mL of 0.9% sodium chloride solution for injection. Withdraw 5mL of the reconstituted solution and administer as an intravenous injection over no less than 3 minutes.

The reconstituted solution should be stored at room temperature up to 30°C and administered within 12 hours after reconstitution.

Intravenous Infusion (20 or 40mg)
A solution for intravenous infusion is prepared by first reconstituting the contents of one vial with 5mL of 0.9% sodium chloride solution for injection, Lactated Ringer's injection or 5% dextrose injection and further diluting the resulting solution to a final volume of 100mL. The solution (admixture) should be administered as an intravenous infusion over a period of 10 to 30 minutes.

The admixture should be stored at room temperature up to 30°C and should be administered within the designated time period as listed in the table below.

Diluent	Administer within
0.9% Sodium Chloride solution for injection	12 hours
Lactated Ringer's injection	12 hours
5% Dextrose injection	6 hours

Any unused solution should be discarded.

ADVERSE REACTIONS
The following adverse drug reactions have been reported during therapy of esomeprazole.

Common: Headache, abdominal pain, diarrhea, flatulence, nausea/vomiting, constipation.
Uncommon: Peripheral oedema, insomnia, dizziness, paresthesia, somnolence.

Rare: Leukopenia, thrombocytopenia, hypersensitivity reactions e.g., fever, angioedema and anaphylactic reaction/shock, hyponatremia, agitation, confusion, depression, taste disturbance, bronchospasm, stomatitis, gastrointestinal candidiasis, hepatitis with or without jaundice, alopecia, photosensitivity, arthralgia, myalgia, malaise, increased sweating.

Very rare: Aggression, hallucinations, hepatic failure, encephalopathy in patients with pre-existing liver disease, erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN), muscular weakness, interstitial nephritis, gynecomastia.

CONTRAINDICATIONS
- Esomeprazole is contraindicated in patients with known hypersensitivity to the active substance esomeprazole or to other substituted benzimidazoles or to any of the excipients of this medicinal product.
- Esomeprazole, like other PPIs, should not be administered with atazanavir.

PRECAUTIONS
General
- In the presence of any alarm symptoms (e.g., significant unintentional weight loss, recurrent vomiting, dysphagia, hematemesis or melaena) and when gastric ulcer is suspected or present, malignancy should be excluded, as treatment with esomeprazole may alleviate symptoms and delay diagnosis.
- Atrophic gastritis has been noted occasionally in gastric corpus biopsies from patients treated long-term with omeprazole, of which esomeprazole is an enantiomer.

Hepatic Insufficient Patients
Dose reduction in patients with severe hepatic disease should be considered.

Renal Insufficient Patients
Patients with severe renal insufficiency should be treated with caution when administered with esomeprazole IV.

Pediatric Patients
The safety and effectiveness of esomeprazole have not been established for pediatric patients.

Drug Interactions
- The decreased intragastric acidity during treatment with esomeprazole might increase or decrease the absorption of drugs if the mechanism of absorption is influenced by gastric acidity. 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.
- 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.
- Patients treated with proton pump inhibitors and warfarin concomitantly may need to be monitored for increases in INR and prothrombin time.

Pregnancy
For esomeprazole, limited data on exposed pregnancies are available. Caution should be exercised when prescribing esomeprazole IV to pregnant women.

Nursing Mothers
It is not known whether esomeprazole is excreted in human breast milk. No studies in lactating women have been performed. Therefore esomeprazole IV should not be used during breast-feeding.

STORAGE
Store below 25°C.
Protect from sunlight and moisture.
Store in carton until the time of use.
Vials can however, be stored, exposed to, at normal indoor light outside the box for up to 24 hours.

The expiration date refers to the product correctly stored at the required conditions.

HOW SUPPLIED
NEXUM IV (Esomeprazole) 40mg lyophilised powder for injection is available as 1 vial plus 5mL sodium chloride solution 0.9% w/v for injection.

Keep out of reach of children.

Please read the contents carefully before use.
This package insert is continually updated from time to time.

Manufactured by:
Getz pharma (PVT) LIMITED
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