NEXPRO

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only

Abbreviated Prescribing information for NEXPRO RD (Esomeprazole Magnesium trihydrate 20 mg/40 mg enteric coated tablet)

[Please refer the complete prescribing information available at www.torrentpharma.com]

PHARMACOLOGICAL PROPERTIES: **Esomeprazole:** It 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.

INDICATION: For the treatment of erosive reflux osaphagaitis prevention of release of oesophagit and helps in eradtcation of H.pyroli associated peptic ulcer.

DOSAGE AND ADMINISTRATION: 40 mg once daily to be taken orally for 4 weeks. An additional 4 weeks treatment is recommended for patients in whom esophagitis has not healed or who have persistent symptoms.

CONTRAINDICATION:. Hypersensitivity to the active substance, to substituted benzimidazoles or to any of the excipients. Esomeprazole should not be used concomitantly with nelfinavir.

WARNINGS & PRECAUTIONS:*Gastrointestinal infections:* Treatment with proton pump inhibitors may lead to slightly increased risk of gastrointestinal infections such as Salmonella and Campylobacter. Absorption of vitamin B12 Esomeprazole, as all acid-blocking medicines, may reduce the absorption of vitamin B12 (cyanocobalamin) due to hypo- or achlorhydria. *Hypomagnesaemia:* 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. *Risk of fracture:* 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. Subacute cutaneous lupus erythematosus (SCLE) Proton pump inhibitors are associated with very infrequent cases of SCLE. If lesions occur, especially in sun-exposed areas of the skin, and if accompanied by arthralgia, the patient should seek medical help promptly and the health care professional should consider stopping NEXPRO. SCLE after previous treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors. *Combination with other medicinal products:* Co-administration of esomeprazole with atazanavir is not recommended. If the combination of atazanavir with a proton pump inhibitor is judged unavoidable, close clinical monitoring is recommended in combination with an increase in the dose of atazanavir to 400 mg with 100 mg of ritonavir; esomeprazole 20 mg should not be exceeded. *Interference with laboratory tests:* 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. If CgA and gastrin levels have not returned to reference range after initial measurement, measurements should be repeated 14 days after cessation of proton pump inhibitor treatment.

DRUG INTERACTION: Methotrexate: 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 mayneed to be considered. Tacrolimus: Concomitant administration of esomeprazole has been reported to increase the serum levels of tacrolimus. A reinforced monitoring of tacrolimus concentrations as well as renal function (creatinine clearance) should be performed, and dosage of tacrolimus adjusted if needed.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. Medicinal products 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. Diazepam: Concomitant administration of 30 mg esomeprazole resulted in a 45% decrease in clearance of the CYP2C19 substrate diazepam. Phenytoin: Concomitant administration of 40 mg esomeprazole resulted in a 13% increase in trough plasma levels of phenytoin in epileptic patients. It is recommended to monitor the plasma concentrations of phenytoin when treatment with esomeprazole is introduced or withdrawn. Voriconazole: Omeprazole (40 mg once daily) increased voriconazole (a CYP2C19 substrate) Cmax and AUC by 15% and 41%, respectively. Cilostazol: Omeprazole as well as esomeprazole act as inhibitors of CYP2C19. Omeprazole, given in doses of 40 mg to healthy subjects in a cross-over study, increased Cmax and AUC for cilostazol by 18% and 26% respectively, and one of its active metabolites by 29% and 69% respectively. Warfarin: Concomitant administration of 40 mg esomeprazole to warfarin-treated patients in a clinical trial showed that coagulation times were within the accepted range. However, post-marketing, a few isolated cases of elevated INR of clinical significance have been reported during concomitant treatment. Monitoring is recommended when initiating and ending concomitant esomeprazole treatment during treatment with warfarin or other coumarine derivatives. Clopidogrel Results from studies in healthy subjects have shown a pharmacokinetic (PK)/ pharmacodynamics (PD) interaction between clopidogrel (300 mg loading dose/75 mg daily maintenance dose) and esomeprazole (40 m p.o.daily) resulting in decreased exposure to the active metabolite of clopidogrel by an average of 40% and resulting in decreased maximum inhibition of (ADP induced) platelet aggregation by an average of 14%. When clopidogrel was given together with a fixed dose combination of esomeprazole 20 mg + ASA 81 mg compared to clopidogrel alone in a study in healthy subjects there was a decreased exposure by almost 40% of the active metabolite of clopidogrel. However, the maximum levels of inhibition of (ADP induced) platelet aggregation in these subjects were the same in the clopidogrel and the clopidogrel + the combined (esomeprazole + ASA) product groups. 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.

ADVERSE REACTIONS: Leukopenia, thrombocytopenia, Agranulocytosis, pancytopenia, Hypersensitivity reactions e.g. fever, angioedema, anaphylactic reaction/shock, Peripheral oedema, Hyponatraemia, Hypomagnesaemia; severe hypomagnesaemia can correlate with hypocalcaemia. Hypomagnesaemia may also be associated with hypokalaemia, Insomnia, Agitation, confusion, depression, Aggression, hallucinations, Headache, Dizziness, paraesthesia, somnolence, Taste disturbance, Blurred vision, Vertigo, Bronchospasm, Abdominal pain, constipation, diarrhoea, benign), Dry mouth, Stomatitis, gastrointestinal candidiasis, Increased liver enzymes Hepatitis with or without jaundice, Hepatic failure, encephalopathy in with pre-existing liver disease, Dermatitis, pruritus, rash, urticarial Alopecia, photosensitivity Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN), Subacute cutaneous lupus erythematosus, Fracture of the hip, wrist or spine, Arthralgia, myalgia, Interstitial nephritis; in some patients renal failure has been reported concomitantly, Acute kidney injury, Muscular weakness, Gynaecomastia, Malaise, increased sweating, and acute kidney injury.

MARKETED BY:

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NEXPRO 20 mg, 40 mg/JUN-20/01/PI
(Additional information is available on request)