NEXIUM® MUPS 20 & 40 mg

esomeprazole

Film-coated tablets

Qualitative and quantitative composition

Each tablet contains 20 mg or 40 mg esomeprazole (as magnesium trihydrate).

For excipients see *List of excipients*.

Pharmaceutical form

Gastro-resistant tablets

20 mg: A light pink, oblong, biconvex, film-coated tablet engraved 20 mg on one side and A EH on the other side.

40 mg: A pink, oblong, biconvex, film-coated tablet engraved 40 mg on one side and A EI on the other side.

Therapeutic indication

NEXIUM MUPS tablets are indicated for:

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).

In combination with an appropriate antibacterial therapeutic regimen for the eradication of Helicobacter pylori and

- Healing of *Helicobacter pylori* associated duodenal ulcer.

Patients requiring continued non-steroidal anti-inflammatory (NSAID) therapy

- Healing of gastric ulcers associated with NSAID therapy.
- Prevention of gastric and duodenal ulcers associated with continuous NSAID therapy in patient at risk. Patients are considered to be at risk due to their age (>60) and documented history of peptic ulcer. Controlled studies do not extend beyond 6 months.

Maintenance of haemostasis and prevention of rebleeding of gastric or duodenal ulcers following treatment with NEXIUM for solution for infusion.

Treatment of Zollinger Ellison Syndrome.

Posology and method of administration

The tablets should be swallowed whole with liquid. They should not be chewed or crushed.

For patients who have difficulty in swallowing the tablets can also be dispersed in half a glass of non-carbonated water. No other liquids should be used as the enteric coating may be dissolved. Stir until the tablets disintegrate and drink the liquid with the pellets immediately or within 30 minutes. Rinse the glass with half a glass of water and drink. The pellets must not be chewed or crushed.

For patients who cannot swallow, the tablets can be dispersed in non-carbonated water and administered through a gastric tube. It is important that the appropriateness of the selected syringe and tube is carefully tested.

For preparation and administration instructions see section *Instructions for use and handling*.

Adults

Gastroesophageal Reflux Disease (GERD)

- treatment of erosive reflux esophagitis
  40 mg once daily for 4 weeks.
  An additional 4 weeks treatment is recommended for patients in whom esophagitis has not healed or who have persistent symptoms. NEXIUM MUPS 40 mg should only be administered for patients with mucosal break of grade C and D under the LA classification system, the grade of which should be confirmed by endoscopical or radiological diagnosis. Patients who have GERD with erosive esophagitis of Grade A and B are recommended to be treated with NEXIUM MUPS 20 mg.

- long-term management of patients with healed esophagitis to prevent relapse
  20 mg once daily.

- symptomatic treatment of (GERD)
  20 mg once daily in patients without esophagitis. If symptom control has not been achieved after 4 weeks, the patient should be further investigated. Once symptoms have resolved, subsequent symptom control can be achieved using 20 mg once daily. In adults, an on demand regimen taking 20 mg once daily, when needed, can be used. In NSAID treated patients at risk of developing gastric and duodenal ulcers, subsequent symptom control using an on demand regimen is not recommended.

In combination with an appropriate antibacterial therapeutic regimen for the eradication of Helicobacter pylori and

- healing of *Helicobacter pylori* associated duodenal ulcer
  20 mg NEXIUM MUPS with 1 g amoxicillin and 500 mg clarithromycin, all twice daily for 7 days.

Patients requiring continued NSAID therapy

Healing of gastric ulcers associated with NSAID therapy: The usual dose is 20 mg once daily. The treatment duration is 4-8 weeks. Prevention of gastric and duodenal ulcers associated with NSAID therapy in patients at risk: 20 mg once daily.

Maintenance of haemostasis and prevention of rebleeding of gastric or duodenal ulcers following treatment with NEXIUM for infusion

40 mg once daily for 7 days to 30 days depending on risk of re-bleeding. The oral treatment period should be preceded by acid-suppression therapy with NEXIUM for infusion 80 mg administered as a bolus infusion over 30 minutes followed by a continuous intravenous infusion of 8 mg/h given over 3 days (72 h), see prescribing information for NEXIUM powder for solution for injection and infusion.

Treatment of Zollinger Ellison Syndrome

The recommended initial dosage is NEXIUM MUPS 40 mg twice daily. The dosage should then be individually adjusted and treatment continued as long as clinically indicated. Based on the clinical data

available, the majority of patients can be controlled on doses between 80 to 160 mg esomeprazole daily. With doses above 80 mg daily, the dose should be divided and given twice daily.

Children 12-18 years

Gastroesophageal Reflux Disease (GERD)

- symptomatic treatment of gastroesophageal reflux disease (GERD)
  20 mg once daily in patients without esophagitis. If symptom control has not been achieved after 4 weeks, the patient should be further investigated. Once symptoms have resolved, subsequent symptom control can be achieved using 20 mg once daily, under medical supervision.

Children below the age of 12 years

NEXIUM MUPS should not be used in children younger than 12 years since no data is available.

Impaired renal function

Dose adjustment is not required in patients with impaired renal function. Due to limited experience in patients with severe renal insufficiency, such patients should be treated with caution (see *Pharmacokinetic properties*).

Impaired hepatic function

Dose adjustment is not required in patients with mild to moderate liver impairment. For patients with severe liver impairment, a maximum dose of 20 mg NEXIUM MUPS should not be exceeded (see *Pharmacokinetic properties*).

Elderly

Dose adjustment is not required in the elderly.

Contraindications

Known hypersensitivity to esomeprazole, substituted benzimidazoles or any other constituents of the formulation.

Concomitant administration with esomeprazole and drugs such as atazanavir and nelfinavir is not recommended (see section *Interactions with other medicinal products and other forms of interaction*).

Special warnings and special precautions for use

In the presence of any alarm symptom (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 NEXIUM MUPS 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.

Patients on on-demand treatment should be instructed to contact their physician if their symptoms change in character. When prescribing NEXIUM MUPS for on demand therapy, the implications for interactions with other pharmaceuticals, due to fluctuating plasma concentrations of esomeprazole should be considered (see *Interactions with other medicinal products and other forms of interaction*).

When prescribing NEXIUM MUPS for eradication of *Helicobacter pylori* possible drug interactions for all components in the triple therapy should be considered. Clarithromycin is a potent inhibitor of CYP3A4 and

hence contraindications and interactions for clarithromycin should be considered when the triple therapy is used in patients concurrently taking other drugs metabolised via CYP3A4 such as cisapride.

Results from studies in healthy subjects have shown a pharmacokinetic/pharmacodynamic interaction between clopidogrel (300 mg loading dose/75 mg daily maintenance dose) and esomeprazole (40 mg 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%. Based on these data, concomitant use of esomeprazole and clopidogrel should be avoided (see also *Interaction with other medicinal products and other forms of interaction*).

Some published observational studies suggest that proton pump inhibitor (PPI) therapy may be associated with a small increased risk for osteoporosis related fractures. However, in other similar observational studies no such increased risk was found.

In AstraZeneca's randomized, double-blind and controlled clinical studies on omeprazole and esomeprazole (including two open long-term studies of up to more than 12 years) there are no indications that PPIs are associated with osteoporotic fractures.

Although a causal relationship between omeprazole/esomeprazole and osteoporotic fractures has not been established, patients at risk for developing osteoporosis or osteoporotic fractures are advised to have appropriate clinical monitoring in accordance with current clinical guidelines for these conditions.

This medicinal product contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

Interactions with other medicinal products and other forms of interaction

Effects of esomeprazole on the pharmacokinetics of other drugs

The gastric acid suppresion during treatment with esomeprazole and other PPIs might decrease or increase the absorption of drugs with a gastric pH dependent absorption. Like with other drugs that decrease the intragastric acidity, the absorption of drugs, such as ketoconazole, itraconazole and erlotinib can decrease while the absorption of drugs such as digoxin can increase during treatment with esomeprazole. Concomitant treatment with omeprazole (20 mg daily) and digoxin in healthy subjects increased the bioavailability of digoxin by 10% (up to 30% in two out of ten subjects).

Esomeprazole inhibits CYP2C19, the major esomeprazole metabolising enzyme. Concomitant administration of 30 mg esomeprazole resulted in a 45% decrease in clearance of the CYP2C19 substrate diazepam. This interaction is unlikely to be of clinical relevance. Concomitant administration of 40 mg esomeprazole resulted in a 13% increase in trough plasma levels of phenytoin in epileptic patients; dose adjustment was not required in this study. Concomitant administration of 40 mg esomeprazole to warfarin-treated patients showed that despite a slight elevation in the trough plasma concentration of the less potent R-isomer of warfarin, the coagulation times were within the accepted rang. However, from post-marketed use cases of elevated INR of clinical significance have been reported during concomitant treatment. Close monitoring is recommended when initiating and ending concomitant esomeprazole treatment during treatment with warfarin or other coumarine derivatives.

Results from studies in healthy subjects have shown a pharmacokinetic/pharmacodynamic interaction between clopidogrel (300 mg loading dose/75mg daily maintenance dose) and esomeprazole (40 mg 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%.

It is, however, uncertain to what extent this interaction is clinically important. One prospective, randomized (but incomplete) study (in over 3760 patients comparing placebo with omeprazole 20 mg in patients treated with clopidogrel and ASA) and non-randomized, post-hoc analyses of data from large, prospective, randomized clinical outcome studies (in over 47000 patients) did not show any evidence of an increased risk for adverse cardiovascular outcome when clopidogrel and PPIs, including esomeprazole, were given concomitantly.

Results from a number of observational studies are inconsistent with regard to increased risk or no increased risk for CV thromboembolic events when clopidogrel is given together with a PPI.

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, likely due to the concomitant administration of low dose ASA.

Omeprazole as well as esomeprazole act as inhibitors of CYP 2C19. Omeprazole, given in doses of 40 mg to healthy subjects in a cross-over study, increased C_{max} and AUC for cilostazol by 18% and 26% respectively, and one of its active metabolites by 29% and 69%, respectively.

In healthy volunteers, concomitant administration of 40 mg esomeprazole resulted in a 32% increase in area under the plasma concentration-time curve (AUC) and a 31% prolongation of elimination half-life (t1/2) but no significant increase in peak plasma levels of cisapride. The slightly prolonged QTc interval observed after administration of cisapride alone, was not further prolonged when cisapride was given in combination with esomeprazole (see *Special warnings and special precautions for use*).

Concomitant administration of esomeprazole has been reported to increase the serum levels of tacrolimus.

When given together with proton pump inhibitors, methotrexate levels have been reported to increase in some patients. In high-dose methotrexate administration a temporary withdrawal of esomeprazole may need to be considered.

Omeprazole has been reported to interact with some antiretroviral drugs. The clinical importance and the mechanisms behind these reported interactions are not always known. Increased gastric pH during omeprazole treatment may change the absorption of the antiretroviral drug. Other possible interaction mechanisms are via CYP 2C19. For some antiretroviral drugs, such as atazanavir and nelfinavir, decreased serum levels have been reported when given together with omeprazole and concomitant administration is not recommended. For other antiretroviral drugs, such as saquinavir, increased serum levels have been reported. There are also some antiretroviral drugs for which unchanged serum levels have been reported when given with omeprazole. Due to the similar pharmacodynamic effects and pharmacokinetic properties of omeprazole and esomeprazole, concomitant administration with esomeprazole and antiretroviral drugs such as atazanavir and nelfinavir is not recommended (see section *Contraindications*).

Esomeprazole has been shown to have no clinically relevant effects on the pharmacokinetics of amoxicillin or quinidine.

Studies evaluating concomitant administration of esomeprazole and either naproxen (non-selective NSAID) or rofecoxib (COX-2-selective NSAID) did not identify any clinically relevant pharmacokinetic interactions during short-term studies.

Effects of other drugs on the pharmacokinetics of esomeprazole
Esomeprazole is metabolised by CYP2C19 and CYP3A4. Concomitant administration of esomeprazole and a CYP3A4 inhibitor, clarithromycin (500 mg b.i.d.), resulted in a doubling of the exposure (AUC) to esomeprazole. 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. However, dose adjustment of esomeprazole is not required in either of these situations.

Drugs known to induce CYP2C19 or CYP3A4 or both (such as rifampicin and St. John's wort) may lead to decreased esomeprazole serum levels by increasing the esomeprazole metabolism.

Pregnancy and lactation
For NEXIUM MUPS , limited clinical data on exposed pregnancies are available. Animal studies with esomeprazole do not indicate direct or indirect harmful effects with respect to embryonal/ fetal development. Animal studies with the racemic mixture do not indicate direct or indirect harmful effects with respect to pregnancy, parturition or postnatal development. Caution should be exercised when prescribing to pregnant women.

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

Effects on ability to drive and use machines
NEXIUM MUPS is not likely to affect the ability to drive or use machines.

Undesirable effects
The following definitions of frequencies are used:

Common	≥1/100
Uncommon	≥1/1000 and <1/100
Rare	≥1/10000 and <1/1000
Very rare	<1/10000

The following adverse drug reactions have been identified or suspected in the clinical trials programme for esomeprazole and/or from post-marketing use. None was found to be dose-related.

Blood and lymphatic system disorders
Rare : Leukopenia, thrombocytopenia
Very rare : Agranulocytosis, pancytopenia

Immune system disorders
Rare : Hypersensitivity reactions e.g. angioedema and anaphylactic reaction/ shock

Metabolism and nutrition disorders
Uncommon : Peripheral oedema

Rare : Hyponatraemia
Very Rare : Hypomagnesaemia; severe hypomagnesaemia may result in hypocalcaemia. Hypomagnesaemia may also result in hypokalaemia.

Psychiatric disorders
Uncommon : Insomnia
Rare : Agitation, confusion, depression
Very rare : Aggression, hallucinations

Nervous system disorders
Common : Headache
Uncommon : Dizziness, paraesthesia, somnolence
Rare : Taste disturbance

Eye disorders
Rare : Blurred vision

Ear and labyrinth disorders
Uncommon : Vertigo

Respiratory, thoracic and mediastinal disorders
Rare : Bronchospasm

Gastrointestinal disorders
Common : Abdominal pain, diarrhoea, flatulence, nausea/ vomiting, constipation,
Uncommon : Dry mouth
Rare : Stomatitis, gastrointestinal candidiasis
Very rare : Microscopic colitis

Hepatobiliary disorders
Uncommon : Increased liver enzymes
Rare : Hepatitis with or without jaundice
Very rare : Hepatic failure, hepatic encephalopathy

Skin and subcutaneous tissue disorders
Uncommon : Dermatitis, pruritus, rash, urticaria
Rare : Alopecia, photosensitivity
Very rare : Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN), acute generalized exanthematous pustulosis (AGEP), drug rash with eosinophilia and systemic symptoms (DRESS).

Musculoskeletal, connective tissue and bone disorders
Rare : Arthralgia, myalgia
Very rare : Muscular weakness

Renal and urinary disorders
Very rare : Interstitial nephritis

Reproductive system and breast disorders
Very rare : Gynaecomastia

General disorders and administration site conditions
Rare : Malaise, hyperhidrosis

Overdose
The symptoms described in connection with deliberate NEXIUM MUPS overdose (limited experience of doses in excess of 240 mg/day) are transient. Single doses of 80 mg esomeprazole were uneventful. No specific antidote is known. Esomeprazole is extensively plasma protein bound and is therefore not readily dialyzable. As in any case of overdose, treatment should be symptomatic and general supportive measures should be utilised.

Pharmacological properties
Pharmacodynamic properties
Pharmacotherapeutic group: proton pump inhibitor
ATC Code: A02B C05

Esomeprazole is the S-isomer of omeprazole and reduces gastric acid secretion through a specific targeted mechanism of action. It is a specific inhibitor of the acid pump in the parietal cell. Both the R- and S-isomer of omeprazole have similar pharmacodynamic activity.

Site and 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.

Effect on gastric acid secretion
After oral dosing with esomeprazole 20 mg and 40 mg the onset of effect occurs within one hour. After repeated administration with 20 mg esomeprazole once daily for five days, mean peak acid output after pentagastrin stimulation is decreased 90% when measured 6 - 7 hours after dosing on day 5.

After 5 days of oral dosing with 20 mg and 40 mg of esomeprazole, intragastric pH above 4 was maintained for a mean time of 13 hours and 17 hours, respectively over 24 hours in symptomatic GERD patients. The proportion of patients maintaining an intragastric pH above 4 for at least 8, 12 and 16 hours respectively were for esomeprazole 20 mg 76%, 54% and 24%. Corresponding proportions for esomeprazole 40 mg were 97%, 92% and 56%.

Using AUC as a surrogate parameter for plasma concentration, a relationship between inhibition of acid secretion and exposure has been shown.

Therapeutic effects of acid inhibition
Healing of reflux esophagitis with esomeprazole 40 mg occurs in approximately 78% of patients after four weeks, and in 93% after 8 weeks.

One week treatment with esomeprazole 20 mg b.i.d. and appropriate antibiotics, results in successful eradication of Helicobacter pylori in approximately 90% of patients.

After eradication treatment for one week there is no need for subsequent monotherapy with antisecretory drugs for effective ulcer healing and symptom resolution in uncomplicated duodenal ulcers.

In a randomized, double blind, placebo-controlled clinical study, 764 patients who presented with endoscopically confirmed peptic ulcer bleeding were randomized to receive NEXIUM solution for infusion (n=375) or placebo (n=389). Following endoscopic hemostasis, patients received either 80 mg esomeprazole as an intravenous infusion over 30 minutes followed by a continuous infusion of 8 mg per hour or placebo for 72 hours. After the initial 72 hour period, all patients received 40 mg oral NEXIUM MUPS for 27 days for acid suppression The occurrence of rebleeding within 3 days was 5.9% in the NEXIUM IV treated group compared to 10.3% for the placebo group (p=0.0256). At 7 and 30 days post-treatment, the occurrence of rebleeding in the NEXIUM MUPS treated versus the placebo treated group was 7.2% vs 12.9% (p=0.0096) and 7.7% vs 13.6%, respectively (p=0.0092).

Other effects related to acid inhibition
During treatment with antisecretory drugs serum gastrin increases in response to the decreased acid secretion. Also chromogranin A (CgA) increases due to decreased gastric acidity. The increased CgA level may interfere with investigations for neuroendocrine tumours. Literature reports indicate that proton pump inhibitor treatment should be stopped 5 to 14 days before CgA measurement**.** Measurements should be repeated if levels have not normalised by this time.

An increased number of ECL cells possibly related to the increased serum gastrin levels, have been observed in some patients during long term treatment with esomeprazole. The findings are considered to be of no clinical significance.

During long-term treatment with antisecretory drugs gastric glandular cysts have been reported to occur at a somewhat increased frequency. These changes are a physiological consequence of pronounced inhibition of acid secretion, are benign and appear to be reversible.

Decreased gastric acidity due to any means including proton pump inhibitors, increases gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with proton pump inhibitors may lead to slightly increased risk of gastrointestinal infections such as *Salmonella* and *Campylobacter* and, in hospitalized patients, possibly also *Clostridium difficile*.

In two studies with ranitidine as an active comparator, NEXIUM MUPS showed better effect in healing of gastric ulcers in patients using NSAIDs, including COX-2 selective NSAIDs.

In two studies with placebo as comparator, NEXIUM MUPS showed better effect in the prevention of gastric and duodenal ulcers in patients using NSAIDs (aged>60 and/ or with previous ulcer), including COX-2 selective NSAIDs.

Pharmacokinetic properties
Absorption and distribution
Esomeprazole is acid labile and is administered orally as enteric-coated granules. *In vivo* conversion to the R-isomer is negligible. Absorption of esomeprazole is rapid, with peak plasma levels occurring approximately 1-2 hours after dose. The absolute bioavailability is 64% after a single dose of 40 mg and increases to 89% after repeated once-daily administration. For 20 mg esomeprazole the corresponding values are 50% and 68%, respectively. The apparent volume of distribution at steady state in healthy subjects is approximately 0.22 L/ kg body weight. Esomeprazole is 97% plasma protein bound.

Food intake both delays and decreases the absorption of esomeprazole although this has no significant influence on the effect of esomeprazole on intragastric acidity.

Metabolism and excretion
Esomeprazole is completely metabolised 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.

The parameters below reflect mainly the pharmacokinetics in individuals with a functional CYP2C19 enzyme, extensive metabolisers.

Total plasma clearance is about 17 L/h after a single dose and about 9 L/h after repeated administration. The plasma elimination half-life is about 1.3 hours after repeated once-daily dosing. The area under the plasma concentration-time curve increases with repeated administration of esomeprazole. This increase is dose-dependent and results in a non-linear dose-AUC relationship after repeated administration. This time - and dose - dependency is due to a decrease of first pass metabolism and systemic clearance probably caused by an inhibition of the CYP2C19 enzyme by esomeprazole and/ or its sulphone metabolite. Esomeprazole is completely eliminated from plasma between doses with no tendency for accumulation during once-daily administration.

The major metabolites of esomeprazole have no effect on gastric acid secretion. Almost 80% of an oral dose of esomeprazole is excreted as metabolites in the urine, the remainder in the faeces. Less than 1% of the parent drug is found in urine.

Special patient populations
Approximately 3% of the population lack a functional CYP2C19 enzyme and are called poor metabolisers. In these individuals the metabolism of esomeprazole is probably mainly catalysed by CYP3A4. After repeated once-daily administration of 40 mg esomeprazole, the mean area under the plasma concentration-time curve was approximately 100% higher in poor metabolisers than in subjects having a functional CYP2C19 enzyme (extensive metabolisers). Mean peak plasma concentrations were increased by about 60%. These findings have no implications for the posology of NEXIUM MUPS . The metabolism of esomeprazole is not significantly changed in elderly subjects (71-80 years of age).

Following a single dose of 40 mg esomeprazole the mean area under the plasma concentration-time curve is approximately 30% higher in females than in males. No gender difference is seen after repeated once-daily administration. These findings have no implications for the posology of NEXIUM MUPS .

Impaired organ function
The metabolism of esomeprazole in patients with mild to moderate liver impairment may be impaired. The metabolic rate is decreased in patients with severe liver impairment resulting in a doubling of the area under the plasma concentration-time curve of esomeprazole. Therefore, a maximum of 20 mg should not be exceeded in patients with severe hepatic impairment. Esomeprazole or its major metabolites do not show any tendency to accumulate with once-daily dosing.

No studies have been performed in patients with decreased renal function. Since the kidney is responsible for the excretion of the metabolites of esomeprazole but not for the elimination of the parent compound, the metabolism of esomeprazole is not expected to be changed in patients with impaired renal function.

Paediatric:
Children 12-18 years:
Following repeated dose administration of 20 mg and 40 mg esomeprazole, the total exposure (AUC) and the time to reach maximum plasma drug concentration (t max) in 12 to18 year-olds was similar to that in adults for both esomeprazole doses.

Preclinical safety data
Preclinical studies reveal no particular hazard for humans, based on conventional studies of single and repeated dose toxicity, embryo-foetal toxicity and mutagenicity. Oral carcinogenicity studies in the rat with the racemic mixture have shown gastric ECL-cell hyperplasia and carcinoids. These gastric effects are the result of sustained, pronounced hypergastrinaemia secondary to reduced production of gastric acid, and are observed after long-term treatment in the rat with inhibitors of gastric acid secretion.

List of excipients
Glycerol monostearate 40-55, hyprolose, hypromellose, iron oxide (20 mg & 40 mg tablets: reddish-brown; 20 mg tablets: yellow) (E 172), magnesium stearate, methacrylic acid ethylacrylate copolymer (I:I) dispersion 30 per cent, cellulose microcrystalline, synthetic paraffin, macrogols, polysorbate 80, crospovidone, sodium stearyl fumarate, sugar spheres (sucrose and maize starch), talc, titanium dioxide (E 171), triethyl citrate.

Incompatibilities
Not applicable

Shelf life
Please refer to expiry date on the blister or outer carton.

Special precautions for storage
Store in the original package. Do not store above 30°C.

Pack size
NEXIUM® MUPS 20 mg
Box of 3 blisters @ 10 film coated tablets (Reg. No.: DKI1335300317A1)

NEXIUM® MUPS 40 mg
Box of 2 blisters @ 7 film coated tablets (Reg. No.: DKI1335300317B1)
Box of 2 blisters @ 15 film coated tablets (Reg. No.: DKI1335300317B1)

Instructions for use and handling

Administration through gastric tube

1. Put the tablet into an appropriate syringe and fill the syringe with approximately 25 mL water and approximately 5 mL air. For some tubes, dispersion in 50 mL water is needed to prevent the pellets from clogging the tube.
2. Immediately shake the syringe for approximately 2 minute to disperse the tablet.
3. Hold the syringe with the tip up and check that the tip has not clogged.
4. Attach the syringe to the tube whilst maintaining the above position.
5. Shake the syringe and position it with the tip pointing down. Immediately inject 5-10 mL into the tube. Invert the syringe after injection and shake (the syringe must be held with the tip pointing up to avoid clogging of the tip).
6. Turn the syringe with the tip down and immediately inject another 5-10 mL into the tube. Repeat this procedure until the syringe is empty.
7. Fill the syringe with 25 mL of water and 5 mL of air and repeat step 5 if necessary to wash down any sediment left in the syringe. For some tubes, 50 mL water is needed.

HARUS DENGAN RESEP DOKTER

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