Reproductive system and breast disorders	Very Rare	Gynaecomastia
General disorders and administration site conditions	Rare	Malaise, increased sweating

Overdose
There is very limited experience to date with deliberate overdose. The symptoms described in connection with 280 mg were gastrointestinal symptoms and weakness. 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 utilized.

Dosage and method of administration
- The capsules should be swallowed whole with liquid. The capsules should not be chewed or crushed.
- For patients who have difficulty in swallowing, the capsules can be opened and their content dispersed in half a glass of non-carbonated water. No other liquids should be used as the enteric coating may be dissolved. Stir and drink the liquid with the granules immediately or within 30 minutes. Rinse the glass with half a glass of water and drink. The granules must not be chewed or crushed.
- For patients who cannot swallow, the content of the capsules 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.

Administration through gastric tube
1. Add the contents of a capsule into approximately 25 ml or 50 ml of water (For some tubes, dispersion in 50 ml water is needed to prevent the granules from clogging the tube).Stir.
2. Draw the suspension into a syringe and add approximately 5 ml of air.
3. Immediately shake the syringe for approximately 2 minutes to disperse the granules.
4. Hold the syringe with the tip up and check that the tip has not clogged.
5. Attach the syringe to the tube whilst maintaining the above position.
6. 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).
7. 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.
8. Fill the syringe with 25 ml of water and 5 ml of air and repeat step 6 if necessary to wash down any sediment left in the syringe. For some tubes, 50 ml water is needed.

Any unused product or waste material should be disposed of in accordance with local requirements.

Special precautions for disposal No special requirements

Adults and adolescents from the age of 12 years
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.
- long-term management of patients with healed esophagitis to prevent relapse: 20 mg once daily.
- 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. 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.

Adults
In combination with appropriate antibacterial therapeutic regimens for the eradication of Helicobacter pylori and
- healing of *Helicobacter pylori* associated duodenal ulcer and
- prevention of relapse of peptic ulcers in patients with Helicobacter pylori associated ulcers.

20 mg esomeprazole 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.

Prolonged treatment after IV induced prevention of re-bleeding of peptic ulcers.
40 mg once daily for 4 weeks after IV induced prevention of re-bleeding of peptic ulcers.

Treatment of Zollinger Ellison Syndrome
The recommended initial dosage is 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 below the age of 12 years
Esomeprazole 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.

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 esomeprazole should not be exceeded.

Elderly
Dose adjustment is not required in the elderly.

Caution: Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph

Registration Number: 20mg (DR-XY41575); 40mg (DR-XY41574)
Date of First Authorization: January 2013 (20mg & 40mg)
Date of Revision: July 2017

STORE BELOW 25°C. Store in the original package in order to protect from moisture.

Availability
Alu-Alu/ blister pack x 7 capsules (box of 14 capsules)

Manufactured by
Ethypharm
Z.I. de Saint Arnoult,
28170 Châteauneuf en Thymerais,
France
For STADApharm, GmbH
Stadastrasse 2-18
61118 Bad Vilbel, Germany

Imported and Distributed by
Natrapharm,Inc.
The Patriot Building
Km. 18 West Service Road,
SLEX, Sucat, Parañaque City

Packed by
Lloyd Laboratories, Inc.
FBIC, Malolos City, Bulacan
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STADA Pharmaceuticals (Asia) Ltd.
Kowloon, Hongkong

NTPZCALL000IN1701

Natrapharm

ESOMEPRAZOLE Magnesium

Peprazom®

Proton Pump Inhibitor
20 mg Delayed-Release Capsule
40 mg Delayed-Release Capsule

Formulation
Each delayed-release capsule contains:
Esomeprazole (as magnesium dihydrate).....20mg
Esomeprazole (as magnesium dihydrate).....40mg

Indications
- 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 appropriate antibacterial therapeutic regimens for the eradication of *Helicobacter pylori* and
  - healing of *Helicobacter pylori* associated duodenal ulcer and
  - prevention of relapse of peptic ulcers in patients with *Helicobacter pylori* associated ulcers
- Patients requiring continued NSAID therapy
- Healing of gastric ulcers associated with NSAID therapy
- Prevention of gastric and duodenal ulcers associated with NSAID therapy, in patients at risk
- Prolonged treatment after IV induced prevention of re-bleeding of peptic ulcers
- Treatment of Zollinger Ellison Syndrome

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 five.

After five 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 eight weeks.

One week treatment with esomeprazole 20 mg twice daily and appropriate antibiotics, results in successful eradication of *H. 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, patients with endoscopically confirmed peptic ulcer bleeding characterized as Forrest Ia, Ib, IIa or IIb (9%, 13%, 38% and 10 % respectively) were randomized to receive esomeprazole 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 open-label 40 mg oral esomeprazole for 27 days for acid suppression. The occurrence of rebleeding within 3 days was 5.9% in the esomeprazole treated group compared to 10.3% for the placebo group. At 30 days post-treatment, the occurrence of rebleeding in the esomeprazole treated versus the placebo treated group 7.7% vs 13.6%.

Other effects related to acid inhibition
During treatment with antisecretory drugs serum gastrin increases in response to the decreased acid secretion.

An increased number of ECL (Enterochromaffin-like) cells possibly related to the increased serum gastrin levels, has been observed in some patients during long term treatment with esomeprazole.

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.*

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

In two studies with placebo as comparator, esomeprazole 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.