Pumpinox®
Esomeprazole
Tablets 20mg and 40mg

Composition
Pumpinox® 20: Each tablet contains 20mg esomeprazole (as magnesium trihydrate).

Pumpinox® 40: Each tablet contains 40mg esomeprazole (as magnesium trihydrate).

Clinical properties
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.

Indications
Pumpinox 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*
- healing of *Helicobacter pylori* associated duodenal ulcer.
- 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.

Posology and method of administration
The tablets should be swallowed whole with liquid. The tablets 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.

Gastroesophageal Reflux Disease (GERD)

- Treatment of erosive reflux esophagitis: 40mg 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: 20mg once daily.
- Symptomatic treatment of gastroesophageal reflux disease (GERD):
  20mg once daily in patients without esophagitis. If symptom control has not been achieved after four weeks, the patient should be further investigated. Once symptoms have resolved, subsequent symptom control can be achieved using an on demand regimen taking 20mg once daily, when needed.

In combination with an appropriate antibacterial therapeutic regimen 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: 20mg Pumpinox with 1g amoxicillin and 500mg clarithromycin, all twice daily for 7 days.

Patients requiring continued NSAID therapy

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

Children
Esomeprazole should not be used in children 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 20mg esomeprazole should not be exceeded.

Elderly
Dose adjustment is not required in the elderly.

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

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 esomprazole 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 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* possible drug interactions for all 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.

Interaction
Effects of esomeprazole on the pharmacokinetics of other drugs.
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 metabolizing enzyme. Thus, when esomeprazole is combined with drugs metabolized 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. Concomitant administration of 30mg esomeprazole resulted in a 45% decrease in clearance of the CYP2C19 substrate diazepam. Concomitant adminstration of 40mg 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. Concomitant administration of 40mg 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 (International Normalized Ratio) of clinical significance have been reported during concomitant

treatment. Monitoring is recommended when initiating and ending concomitant treatment.
In healthy volunteers, concomitant administration of 40mg 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.

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 or rofecoxib did not identify and clinically relevant pharmacokinetic interactions during short-term studies.

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

Pregnancy and lactation
For esomeprazole, clinical data on exposed pregnancies are insufficient. With the recemic mixture omeprazole data on a larger number of exposed pregnancies from epidemiological studies indicate no malformative nor foetotoxic effects. 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 esomeprazole should not be used during breast-feeding.

Effects on ability to drive and use machines
No effects have been observed.

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

Common (>1/100, <1/10)	Headache, abdominal pain, diarrhoea, flatulence, nausea/vomiting, constipation.
Uncommon (>1/1000, <1/100)	Dermatitis, pruritus, urticaria, dizziness, dry mouth.
Rare (>1/10000, <1/1000)	Hyerpsensitivity reactions e.g. angioedema, anaphylactic reaction, increased liver enzymes, blurred vision, Stevens Johnson syndrome, erythema multiforme, myalgia

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: Encephalopathy in patients with pre-existing severe liver disease; hepatitis with or without jaundice, hepatic failure.

Musculoskeletal: Arthralgia and muscular weakness.

Skin: Rash, photosensitivity, toxic epidermal necrolysis (TEN), alopecia.

Other: Malaise. Hypersensitivity reactions e.g. fever, bronchospasm and interstitial nephritis. Increased sweating, peripheral oedema, taste disturbance and hyponatraemia.

Overdose

There is very limited experience to date with deliberate overdose. The symptoms described in connection with 280mg were gastrointestinal symptoms and weakness. Single doses of 80mg 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.

Special precautions for storage

Do not store above 30°C. Store in the original package.

Instructions for use and handling

Administration through gastric tube

1. Put the tablet into an appropriate syringe and fill the syringe with approximately 25mL water and approximately 5mL air. For some tubes, dispersion in 50mL water is needed to prevent the pellets from clogging the tube.
2. Immediately shake the syringe for approximately 2 minutes 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.

Presentation

Pumpinox® 20: Available in a pack of 14/tabs.
Pumpinox® 40: Available in a pack of 14/tabs.