Inhibitol®
(Lansoprazole)

Highnoon

COMPOSITION
Inhibitol 30mg Capsule: Each capsule contains:
Lansoprazole (as enteric-coated pellets) 30mg

DESCRIPTION
Lansoprazole is a benzimidazole, a compound that inhibits gastric acid secretion.
It has a prolonged pharmacological action and may provide effective acid suppression over 24 hours.

MECHANISM OF ACTION
Lansoprazole belongs to a class of antisecretory compounds that suppress gastric acid secretion by specific inhibition of the (H^+, K^+)-ATPase enzyme system at the secretory surface of the gastric parietal cell. Because this enzyme system is regarded as the acid (proton) pump within the parietal cell, lansoprazole has been characterized as a gastric acid-pump inhibitor, in that it blocks the final step of acid production. This effect is dose-related and leads to inhibition of both basal and stimulated gastric acid secretion irrespective of the stimulus, Lansoprazole does not exhibit anticholinergic or histamine type-2 antagonist activity.

PHARMACOKINETICS
Lansoprazole is rapidly absorbed after oral doses and peak plasma concentration occurs after 1.5 to 2 hours. Bioavailability is reported to be 80% or more even with the first doses, although the drug must be given in an enteric coated form, since lansoprazole is unstable at acid pH. Food slows the absorption of lansoprazole and reduces the bioavailability by about 50%. Lansoprazole is about 97% bound to plasma protein. It is extensively metabolized in the liver primarily by cytochrome P450 isoenzymes. CYP2C19 to the form of 5-hydroxyl-lansoprazole and by CYP3A4 to form lansoprazole sulfone. Metabolites are excreted mainly in faeces via the bile; only about 15 to 30% of a dose is excreted in the urine. The plasma elimination half-life is around 1 to 2 hours but the duration of the action is much longer. Clearance is decreased in elderly patients and in hepatic impairments.

INDICATIONS
- Treatment of duodenal and gastric ulcer
- Treatment and prophylaxis of reflux oesophagitis
- Treatment of erosive esophagitis
- Maintenance of Healing of erosive esophagitis
- Eradication of Helicobacter pylori (H. pylori) concurrently given with appropriate antibiotic therapy for treatment of H.pylori-associated ulcers
- Treatment of NSAID-associated benign gastric and duodenal ulcers in patients requiring continued NSAID treatment
- Prophylaxis of NSAID-associated gastric ulcers and duodenal ulcers in patients at risk requiring continued therapy
- Symptomatic gastroesophageal reflux disease
- Zollinger-Ellison syndrome
- Acid related dyspepsia

DOSAGE AND ADMINISTRATION
It should be taken once daily except when managing H. pylori eradication when treatment is twice daily.
To achieve the optimal acid inhibitory effect it should be administered in the morning at-least 30 minutes before food. The capsules should be swallowed whole and not crushed or chewed.

Treatment of Duodenal Ulcer
The recommended dose is 30 mg once daily for 2 weeks. In patients not fully healed within this time, the medication is continued at the same dose for another two weeks.

Treatment of Gastric Ulcer
The recommended dose is 30 mg once daily for 4 weeks. The ulcer usually heals within 4 weeks, but in patients not fully healed within this time, the medication may be continued at the same dose for another 4 weeks.

Reflux Oesophagitis
The recommended dose is 30 mg once daily for 4 weeks. In patients not fully healed within this time, the treatment may be continued at the same dose for another 4 weeks.

Prophylaxis of Reflux Oesophagitis
15 mg once daily. The dose may be increased up to 30 mg daily as necessary.

Short-term Treatment of Erosive Esophagitis
30mg once daily for up to 8 weeks. Patients who do not heal after 8 weeks, may be given an additional eight weeks of treatment. If there is a recurrence of erosive esophagitis, an additional eight week course of Lansoprazole may be considered.

Maintenance of Healing Of Erosive Esophagitis
15 mg Once daily.

Eradication of Helicobacter Pylori
When selecting appropriate combination therapy consideration should be given to official local guidance regarding bacterial resistance, duration of treatment, (most commonly 7 days but sometimes up to 14 days), and appropriate use of antibacterial agents.
The recommended dose is 30 mg lansoprazole twice daily for 7 days in combination with one of the following:
clarithromycin 250-500 mg twice daily + amoxicillin 1 g twice daily
clarithromycin 250 mg twice daily + metronidazole 400-500 mg twice daily
H. pylori eradication rates of up to 90%, are obtained when clarithromycin is combined with lansoprazole and amoxicillin or metronidazole.
Six months after successful eradication treatment, the risk of re-infection is low and relapse is therefore unlikely.
Use of a regimen including lansoprazole 30 mg twice daily, amoxicillin 1 g twice daily and metronidazole 400-500 mg twice daily has also been examined. Lower eradication rates were seen using this combination than in regimens involving clarithromycin. It may be suitable for those who are unable to take clarithromycin as part of an eradication therapy, when local resistance rates to metronidazole are low.

Treatment of NSAID associated benign gastric and duodenal ulcers in patients requiring continued NSAID treatment
30 mg once daily for four weeks. In patients not fully healed the treatment may be continued for another four weeks. For patients at risk or with ulcers that are difficult to heal, a longer course of treatment and/or a higher dose should probably be used.

Prophylaxis of NSAID associated gastric and duodenal ulcers in patients at risk (such as age > 65 or history of gastric or duodenal ulcer) requiring prolonged NSAID treatment
15 mg once daily. If the treatment fails the dose 30 mg once daily should be used.

Symptomatic gastro-oesophageal reflux disease
The recommended dose is 15 mg or 30 mg daily. Relief of symptoms is obtained rapidly. Individual adjustment of dosage should be considered. If the symptoms are not relieved within 4 weeks with a daily dose of 30 mg, further examinations are recommended.

Zollinger-Ellison syndrome
The recommended initial dose is 60 mg once daily. The dose should be individually adjusted and the treatment should be continued for as long as necessary. Daily doses of up to 180 mg have been used. If the required daily dose exceeds 120 mg, it should be given in two divided doses.

Acid Related Dyspepsia
15mg to 30mg once daily for 2 to 4 weeks

CONTRAINDICATIONS
- Hypersensitivity to lansoprazole or any component of the inhibitor's formulation. Hypersensitivity reactions may include anaphylaxis, anaphylactic shock, angioedema, bronchospasm, acute tubulointerstitial nephritis, and urticaria.
- Proton Pump Inhibitors (PPIs), lansoprazole, are contraindicated with rilpivirine-containing products.

ADVERSE EVENTS
The reported adverse events are: leucopenia, thrombocytopenia, eosinophilia, anaemia, pancytopenia, agranulocytosis, anaphylactic shock, depression, hallucination, insomnia, confusion, headache, dizziness, paraesthesia, vertigo, restlessness, somnolence, tremor, visual disturbances, vomiting, nausea, diarrhoea, stomach ache, constipation, flatulence, dry mouth or throat, fundic gland polyps (benign), pancreatitis, candidiasis of the oesophagus, glossitis, taste disturbances, colitis, stomatitis, increase in liver enzyme levels, hepatitis, jaundice, urticaria, itching, rash, petechiae, purpura, erythema multiforme, photosensitivity, hair loss, Stevens-Johnson syndrome, toxic epidermal necrolysis, fracture of the hip, wrist or spine, arthralgia, myalgia, interstitial nephritis, gynaecomastia, fatigue, oedema, angioedema, fever, hyperhidrosis, anorexia, impotence, increase in cholesterol and triglyceride levels, hyponatremia, cutaneous and systemic lupus erythematosus, cyanocobalamin (Vitamin B12) deficiency, hypomagnesemia and fundic gland polyps.

DRUG INTERACTIONS
Medicinal Products with Ph Dependent Absorption
Lansoprazole may interfere with the absorption of other medicinal products where gastric pH is an important determinant of oral bioavailability.

HIV Protease Inhibitors
Co-administration of lansoprazole is not recommended with HIV protease inhibitors for which absorption is dependent on acidic intragastric pH, such as atazanavir and nelfinavir, due to significant reduction in their bioavailability.

Ketoconazole and Itraconazole
The absorption of ketoconazole and itraconazole from the gastrointestinal tract is enhanced by the presence of gastric acid. Administration of lansoprazole may result in sub-therapeutic concentrations of ketoconazole and itraconazole and the combination should be avoided.

Digoxin
Co-administration of lansoprazole and digoxin may lead to increased digoxin plasma levels. The plasma levels of digoxin should therefore be monitored and the dose of digoxin adjusted if necessary when initiating and ending lansoprazole treatment.

Medicinal Products Metabolised by P450 Enzymes
Lansoprazole may increase plasma concentrations of medicinal products that are metabolised by CYP3A4. Caution is advised when combining lansoprazole with medicinal products which are metabolised by this enzyme and have a narrow therapeutic window.

Warfarin
There have been reports of increased INR and prothrombin time in patients receiving PPIs and warfarin concomitantly. increase in INR and prothrombin time may lead to abnormal bleeding and even death. Patients treated with lansoprazole and warfarin concomitantly may need to be monitored for increase in INR and prothrombin time.

Theophylline
Lansoprazole reduces the plasma concentration of theophylline, which may decrease the expected clinical effect at the dose. Patient monitoring should be taken in co-administration of lansoprazole with theophylline.

Tacrolimus
Co-administration of lansoprazole increases the plasma concentrations of tacrolimus (a CYP3A and P-gp substrate). Monitoring of tacrolimus plasma concentrations is advised when concomitant treatment with lansoprazole is initiated or ended.

Medicinal products transported by P-glycoprotein
Lansoprazole has been observed to inhibit the transport protein, P-glycoprotein (P-gp) in vitro. The clinical relevance of this is unknown.

Effects of other medicinal products on lansoprazole
Medicinal products which inhibit CYP2C19
Fluvoxamine
A dose reduction may be considered when combining lansoprazole with the CYP2C19 inhibitor fluvoxamine. The plasma concentrations of lansoprazole increase up to 4-fold.

Medicinal products which induces CYP2C19 and CYP3A4
Enzyme inducers affecting CYP2C19 and CYP3A4 such as rifampicin, and St John´s wort (*Hypericum perforatum*) can markedly reduce the plasma concentrations of lansoprazole.

Others
Methotrexate
Concomitant use with high-dose methotrexate may elevate and prolong serum levels of methotrexate and/or its metabolite, possibly leading to methotrexate toxicities.
Sucralfate/Antacids
Sucralfate/Antacids may decrease the bioavailability of lansoprazole. Therefore lansoprazole should be taken at least 1 hour after taking these medicinal products.
Non-steroidal anti-inflammatory medicinal products
No clinically significant interactions of lansoprazole with non-steroidal anti-inflammatory medicinal products have been demonstrated, although no formal interactions studies have been performed.

WARNINGS AND PRECAUTIONS
- In common with other anti-ulcer therapies, the possibility of malignant gastric tumour should be excluded when treating a gastric ulcer with lansoprazole because lansoprazole can mask the symptoms and delay the diagnosis.
- Lansoprazole, like all proton pump inhibitors (PPIs), might increase the counts of bacteria normally present in the gastrointestinal tract. This may increase the risk of gastrointestinal infections caused by bacteria such as Salmonella, Campylobacter and, especially in hospitalized patients, Clostridium difficile.
- Co-administration of lansoprazole is not recommended with HIV protease inhibitors for which absorption is dependent on acidic intragastric pH, such as atazanavir and nelfinavir, due to significant reduction in their bioavailability. If co-administration of lansoprazole with HIV protease inhibitors is unavoidable, close clinical monitoring is recommended.
- Severe hypomagnesaemia has been reported in patients treated with PPIs like lansoprazole 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. In most affected patients, hypomagnesaemia improved after magnesium replacement and discontinuation of the PPI.
- For patients expected to be on prolonged treatment or who take PPIs with digoxin or medicinal products that may cause hypomagnesaemia (e,g., diuretics), health care professionals should consider measuring magnesium levels before starting PPI treatment and periodically during treatment.
- Increased Chromogranin A (CgA) level may interfere with investigations for neuroendocrine tumours. To avoid this interference, Lansoprazole capsules 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.
- Daily treatment with any acid-suppressing medications over a prolonged period of time (several years) may lead to malabsorption of cyanocobalamin (vitamin B12) caused by hypo- or achlorhydria. Cyanocobalamin deficiency should be considered in patients with Zollinger-Ellison syndrome and other pathological hypersecretory conditions requiring long-term treatment, individuals with reduced body stores or risk factors for reduced vitamin B12 absorption (such as the elderly) on long-term therapy or if relevant clinical symptoms are observed.
- Lansoprazole should be used with caution in patients with moderate and severe hepatic dysfunction.
- Decreased gastric acidity due to lansoprazole might be expected to increase gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with lansoprazole may lead to a slightly increased risk of gastrointestinal infections such as *Salmonella* and *Campylobacter*.
- In patients suffering from gastro-duodenal ulcers, the possibility of *H. pylori* infection as an etiological factor should be considered.
- If lansoprazole is used in combination with antibiotics for eradication therapy of *H.pylori*, then the instructions for the use of these antibiotics should also be followed.
- Because of limited safety data for patients on maintenance treatment for longer than 1 year, regular review of the treatment and a thorough risk/benefit assessment should regularly be performed in these patients.
- Very rarely cases of colitis have been reported in patients taking lansoprazole. Therefore, in the case of severe and/or persistent diarrhoea, discontinuation of therapy should be considered.
- With the exception of patients treated for the eradication of *H. pylori* infection, if diarrhoea persists, administration of lansoprazole should be discontinued, due to the possibility of microscopic colitis with thickening of the collagen bundle or infiltration of inflammatory cells noted in the large intestine submucosa. In majority of cases, symptoms of microscopic colitis resolve on discontinuation of lansoprazole.
- The treatment for the prevention of peptic ulceration of patients in need of continuous NSAID treatment should be restricted to high risk patients (e.g. previous gastrointestinal bleeding, perforation or ulcer, advanced age, concomitant use of medication known to increase the likelihood of upper GI adverse events [e.g. corticosteroids or anticoagulants], the presence of a serious co-morbidity factor or the prolonged use of NSAID maximum recommended doses).
- 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 the presence of other recognised risk factors. Observational studies suggest that proton pump inhibitors may increase the overall risk of fracture by 10-40%. Some of this increase may be due to other risk factors. Patients at risk of osteoporosis should receive care according to current clinical guidelines and they should have an adequate intake of vitamin D and calcium.
- 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 Lansoprazole capsules. SCLE after previous treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.
- PPI use is associated with an increased risk of fundic gland polyps that increases with long-term use, especially beyond one year. Most PPI users who developed fundic gland polyps were asymptomatic and fundic gland polyps were identified incidentally on endoscopy. Use the shortest duration of PPI therapy appropriate to the condition being treated.
- Severe cutaneous adverse reactions, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP) have been reported in association with the use of proton pump inhibitors.

USE IN SPECIAL POPULATION
Pregnancy: There is insufficient evidence to recommend the use of lansoprazole in pregnancy. Published observational studies overall do not indicate an association of adverse pregnancy outcomes with lansoprazole treatment.

Lactation: Animal studies indicate that lansoprazole is secreted into breast milk. There is no information on the secretion of lansoprazole into breast milk in humans, However, breast-feeding should be discontinued the use of lansoprazole is considered essential.

Paediatric Use: The safety and effectiveness of lansoprazole has been established in pediatric patients I to 17 years of age for short-term treatment of symptomatic GERD and erosive esophagitis. Use of lansoprazole in this population is supported by evidence from adequate and well-controlled studies. The safety and effectiveness of lansoprazole in patients less than 1 year of age has not been established.

Renal Impairment
There is no need for a dose adjustment in patients with impaired renal function.

Hepatic Impairment
Patients with moderate or severe liver disease should be kept under regular supervision and a 50% reduction of the daily dose is recommended.

Elderly
Due to reduced clearance of lansoprazole in the elderly an adjustment of dose may be necessary based on individual requirements. A daily dose of 30 mg should not be exceeded in the elderly unless there are compelling clinical indications.

OVERDOSAGE
The effects of overdose on lansoprazole in humans are not known (although the acute toxicity is likely to be low) and, consequently, instruction for treatment cannot be given. However, daily doses of up to 180 mg of lansoprazole orally and up to 90 mg of lansoprazole intravenously have been administered in trials without significant undesirable effects.

Lansoprazole is not removed from the circulation by hemodialysis.

DOSAGE AND INSTRUCTIONS
To be sold and used on the prescription of a registered medical practitioner only. Keep out of reach of children. Do not store above 30°C. Keep in a dry place. Protect from light.

PRESENTATION
Inhibitol 30mg Capsules: Alu. PVC. Blister Pack of 2 x 7's.

اِن ہیبٹال®
(لینسوپرازول)

خوراک و ہدایات:
صرف مستند ڈاکٹر کے نسخہ کے مطابق ہی دوا فروخت اور استعمال کی جائے۔
بچوں کی پہنچ سے دور رکھیں۔ 30°C سے زیادہ درجہ حرارت پر نہ رکھیں۔
خشک جگہ پر رکھیں۔ روشنی سے بچائیں۔

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