hovid

VIHORxx-PC2

LANXID-OD Capsule 30 mg

DESCRIPTION
White opaque and white opaque capsule with "LAN30" printed on the cap and "hovid" on the body the capsule; Capsule filled with white off-white spherical pellets.

COMPOSITION
Each capsule contains: Lansoprazole 30 mg.

ACTIONS AND PHARMACOLOGY
Lansoprazole is a selective and irreversible proton pump inhibitor. In the acidic environment of the gastric parietal cell, lansoprazole is converted to active sulphenamide derivatives that bind to the sulfhydryl group of (H+, K+)-adenosine triphosphate [(H+, K+)-ATPase], also known as the proton pump. (H+, K+)-ATPase catalyzes the final step in the gastric acid secretion pathway. Lansoprazole's inhibition of (H+, K+)-ATPase results in inhibition of both centrally and peripherally mediated gastric acid secretion. The inhibitory effect is dose-related. Lansoprazole inhibits both basal and stimulated gastric acid secretion regardless of the stimulus.

PHARMACOKINETICS
Absorption: Since lansoprazole is acid-labile, it is administered as a capsule containing enteric-coated granules to prevent gastric decomposition and to increase bioavailability. Once lansoprazole has left the stomach, absorption is rapid and relatively complete, with absolute bioavailability over 80%. Bioavailability may be decreased if lansoprazole is administered within 30 minutes of food intake as compared to that of a fasting state.

Absorption may be delayed in patients with hepatic cirrhosis.

Distribution: Distributed in tissue, particularly gastric cells. Apparent oral volume of distribution following administration of 30 mg of lansoprazole is about 0.5 liters per kilogram (L/kg).

Protein binding: Very high (around 97%); protein binding remains constant over the concentration range of 0.05 to 5 mcg per mL. In patients with renal function impairment, protein binding may be decreased by 1 to 1.5%.

Half life:
- Normal renal function: Approximately 1.5 hours.
- Renal function impairment: Shortened elimination half-life.
- Elderly patients: 1.9 to 2.9 hours.
- Hepatic function impairment: 3.2 to 7.2 hours.

Elimination:
- **Renal:** approximately 14 to 25 % of a dose of lansoprazole is excreted in the urine, as conjugated and unconjugated hydroxylated metabolites.
  Less than 1% of unchanged lansoprazole is detectable in the urine.
- **Biliary/fecal:** Approximately two-thirds of a dose of lansoprazole is detected as metabolites in the feces.

INDICATIONS
Lansoprazole is indicated for:
- gastroeosphageal reflux disease (GERD) including heartburn and erosive esophangitis
- gastric ulcer
- duodenal ulcer
- hypersecretory conditions including Zollinger-Ellison syndrome

Lansoprazole is also indicated in combination with amoxicillin and/ or clarithromycin for the treatment of duodenal ulcer associated with *H. pylori* infection.

CONTRAINDICATIONS
- Hypersensitivity to the active substance or to any of the excipients.
- Lansoprazole should not be administered with atazanavir.

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 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.
- 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).
- 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 drugs that may cause hypomagnesaemia (e.g., diuretics), health care professionals should consider measuring magnesium levels before starting PPI treatment and periodically during treatment.
- 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. 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.
- **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 <invented name>. SCLE after previous treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.

  As lansoprazole contains sucrose, patients with rare hereditary problems of fructose intolerance, glucosegalactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.
- **Effects on ability to drive and use machines:** Adverse drug reactions such as dizziness, vertigo, visual disturbances and somnolence may occur. Under these conditions the ability to react may be decreased.

PREGNANCY AND LACTATION
Pregnancy: The use of lansoprazole during pregnancy is not recommended.

Lactation: It is not known whether lansoprazole is excreted in human breast milk.

A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with lansoprazole should be made taking into account the benefit of breastfeeding to the child and the benefit of lansoprazole therapy to the woman.

DRUG INTERACTIONS
Effects of lansoprazole on other drugs
Medicinal products with pH dependent absorption
Lansoprazole may interfere with the absorption of drugs where gastric pH is critical to bioavailability.

Atazanavir: Co-administration of lansoprazole (60 mg once daily) with atazanavir 400 mg to healthy volunteers resulted in a substantial reduction in atazanavir exposure (approximately 90% decrease in AUC and C_{max}). Lansoprazole should not be co-administered with atazanavir.

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.

BACK

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 drugs that are metabolised by CYP3A4. Caution is advised when combining lansoprazole with drugs which are metabolised by this enzyme and have a narrow therapeutic window.

Theophylline: Lansoprazole reduces the plasma concentration of theophylline, which may decrease the expected clinical effect at the dose. Caution is advised when combining the two drugs.

Tacrolimus: Co-administration of lansoprazole increases the plasma concentrations of tacrolimus (a CYP3A and Pgp substrate). Lansoprazole exposure increased the mean exposure of tacrolimus by up to 81%.

Monitoring of tacrolimus plasma concentrations is advised when concomitant treatment with lanzoprazole 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*.

Effects of other drugs on lansoprazole
Drugs 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.

Drugs 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
Sucralfate/Antacids: Sucralfate/Antacids may decrease the bioavailability of lansoprazole. Therefore lansoprazole should be taken at least 1 hour after taking these drugs.

No clinically significant interactions of lansoprazole with nonsteroidal anti-inflammatory drugs have been demonstrated, although no formal interactions studies have been performed.

MAIN SIDE/ADVERSE EFFECTS

Frequencies are defined as common; uncommon; rare; very rare, not known.

Blood and lymphatic system disorders
Uncommon: Thrombocytopenia,eosinophilia, leucopenia
Rare: Anaemia
Very rare: Agranulocytosis, pancytopenia

Metabolism and nutritional disorders
Not known: Hypomagnesaemia

Psychiatric Disorders
Uncommon: Depression
Rare: Insomnia, hallucination, confusion

Nervous system Disorders
Common: Headache, dizziness
Rare: Restlessness, vertigo, paresthesia, somnolence, tremor

Eye disorders
Rare: Visual disturbances

Gastrointestinal Disorders
Common: Nausea, diarrhoea, stomach ache, constipation, vomiting, flatulence, dry mouth or throat
Rare: Glossitis, candidiasis of the oesophagus, pancreatitis, taste disturbances
Very rare: Colitis, stomatitis

Hepatobiliary disorders
Common: Increase in liver enzyme levels
Rare: Hepatitis, jaundice

Skin and subcutaneous tissue disorders
Common: Urticaria, itching, rash
Rare: Petechiae, purpura, hair loss, erythema multiforme, photosensitivity
Very rare: Steven-Johnson syndrome, toxic epidermal necrolysis
Not known: Subacute cutaneous lupus erythematosus

Musculoskeletal and connective tissue disorders
Uncommon: Arthralgia, myalgia, Fracture of the hip, wrist or spine

Renal and urinary disorders
Rare: Interstitial nephritis

Reproductive system and breast disorders
Rare: Gynaecomastia

General disorders and administration site conditions
Common: Fatigue
Uncommon: Oedema
Rare: Fever, hyperhidrosis, angioedema, anorexia, impotence
Very rare: Anaphylactic shock

Investigations
Very rare: Increase in cholesterol and triglyceride levels, hyponatremia

OVERDOSE AND TREATMENT

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 without significant undesirable effects.

In the case of suspected overdose the patient should be monitored. Lansoprazole is not significantly eliminated by haemodialysis. If necessary, gastric emptying, charcoal and symptomatic therapy is recommended.

DOSAGE AND ADMINISTRATION

For oral administration.

Adult:
Administer one capsule once daily.
- **Duodenal ulcer:** One capsule once daily for four weeks.
- **Reflux esophagitis:** One capsule once daily for four to eight weeks.
- **Zollinger-Ellison syndrome:** The dosage should be adjusted according to the patient's signs and symptoms.
- **Eradication of *H. pylori:*** One capsule, twice daily plus two of the antibiotics (amoxicillin 1 g twice daily or metronidazole 400 mg twice daily, and clarithromycin 250 mg to 500 mg). The best eradication results are obtained when clarithromycin is combined with either amoxicillin or metronidazole.
- **Acid related dyspepsia:** One capsule once daily for two to four weeks.

Short term treatment for symptomatic GERD and Erosive Esophagitis (12 to 17 years old):
One capsule once daily for up to eight weeks.

Treatment and prophylaxis of NSAID-associated benign gastric ulcers, duodenal ulcers and relief of symptoms in patients requiring continued NSAID treatment:
One capsule once daily for four to eight weeks.

Storage:
Store below 30°C. Protect from light and moisture.

Presentation/Packing:
Blisters of 3 x 10's, 10 x 10's.

Product Registration Holder: HOVID Bhd.
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