LANRIEF ™

Orally disintegrating tablets 15mg/30mg

1. Generic Name: Lansoprazole

2. Qualitative and Quantitative composition:

Each uncoated tablet contains:

Lansoprazole IP..... 15 mg (as enteric coated pellets)

Excipients..... q.s

Colours: Red oxide of iron and Titanium Dioxide IP.

Each uncoated tablet contains:

Lansoprazole IP..... 30 mg (as enteric coated pellets)

Excipients ..... q.s

Colours: Red oxide of iron and Titanium Dioxide IP.

3. Dosage form and strength:

Dosage form: Orally disintegrating tablets is available in oral dosage form.

Strength: Available in 15mg and 30mg

4. Clinical particulars

4.1. Therapeutic indication

Gastroesophageal reflux (GER) / Gastroesophageal reflux disease (GERD) related symptoms and GERD associated Esophagitis in Pediatric patients.

4.2. Posology and method of administration

Lanrief orally disintegrating tablets should be taken as directed by physician or as given below:

Children weighing 30 kg or less should be given 15 mg once daily, and those weighing more than 30 kg should be given 30 mg once daily.

Place the tablet on the tongue and allow it to disintegrate, with or without water, until the particles can be swallowed. Alternatively, the tablets may be swallowed whole with a glass of water or place the tablet in a teaspoonful of water till it gets disintegrated and then administer the content. The tablets should not be crushed or chewed.

4.3. Contraindication

Lanrief orally disintegrating tablets is contraindicated in patients with known severe hypersensitivity to any component of the formulation of Lanrief. Proton Pump Inhibitors (PPIs), including lansoprazole delayed-release orally disintegrating tablets, are contraindicated with rilpivirine-containing products.

4.4. Special warnings and precautions for use:

- **Gastric Malignancy:** Symptomatic response to therapy with lansoprazole does not preclude the presence of gastric malignancy.
- **Clostridium difficile Associated Diarrhea:** May be associated with an increased risk of Clostridium difficile associated diarrhea (CDAD), especially in hospitalized patients.
- **Bone Fracture:** Several published observational studies suggest that PPI therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist or spine. The risk of fracture was increased in patients who received high-dose, defined as multiple daily doses, and long-term PPI therapy (a year or longer). Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the conditions being treated.
- **Hypomagnesemia:** Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPIs for at least three months, in most cases after a year of therapy. Serious adverse events include tetany, arrhythmias, and seizures. In most patients, treatment of hypomagnesemia required magnesium replacement and discontinuation of the PPI. For patients expected to be on prolonged treatment or who take PPIs with medications such as digoxin or drugs that may cause hypomagnesemia (e.g., diuretics), health care professionals may consider monitoring magnesium levels prior to initiation of PPI treatment and periodically.
- **Concomitant Use of Lanrief with Methotrexate**: Literature suggests that concomitant use of PPIs with methotrexate may elevate and prolong serum levels of methotrexate and/or its metabolite, possibly leading to methotrexate toxicities. In high-dose methotrexate administration, a temporary withdrawal of the PPI may be considered in some patients.

4.5. Drug interactions:

- **Atazanavir:** PPIs are likely to substantially decrease the systemic concentrations of the HIV protease inhibitor atazanavir, which is dependent upon the presence of gastric acid for absorption and may result in a loss of therapeutic effect of atazanavir and the development of HIV resistance. Therefore, Lanrief and other PPIs should not be co-administered with atazanavir.

- **Drugs with pH-Dependent Absorption:** PPIs may interfere with the absorption of other drugs where gastric pH is an important determinant of oral bioavailability (e.g., ampicillin esters, digoxin, iron salts, ketoconazole)
- **Warfarin:** Concomitant warfarin use may require monitoring for increases in INR and prothrombin time. 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.
- **Tacrolimus:** Concomitant administration of lansoprazole and tacrolimus may increase whole blood levels of tacrolimus, especially in transplant patients who are intermediate or poor metabolizers of CYP2C19.
- **Theophylline:** Titration of theophylline dosage may be required when concomitant lansoprazole use is started or stopped.
- **Methotrexate:** Lansoprazole may increase serum levels of methotrexate
- **Combination Therapy with Clarithromycin:** Concomitant administration of clarithromycin with other drugs can lead to serious adverse reactions due to drug interactions.

4.6 Use in special population

- **Pediatric:** The safety and effectiveness of lansoprazole have been established in pediatric patients 1 to 17 years of age for short-term treatment of symptomatic GERD and erosive esophagitis, however, lansoprazole was not effective in patients with symptomatic GERD, 1 month to less than 1 year of age in a multicentre, double-blind, placebo-controlled study.
- **Geriatric:** No dosage adjustment of lansoprazole is necessary in geriatric patients. The incidence rates of lansoprazole-associated adverse reactions and laboratory test abnormalities are similar to those seen in younger patients.
- **Hepatic impairment:** Consider dose adjustment in patients with severe Hepatic impairment.
- **Renal failure:** No dosage adjustment of Lanrief is necessary in patients with renal impairment.
- **Pregnancy and lactation:** There are no adequate or well-controlled studies in pregnant women.

4.7. Effects on ability to drive and use machine.

Data not available hence not advisable.

4.8. Undesirable effects:

- **Most commonly reported adverse reactions (≥1%):** diarrhea, abdominal pain, nausea and constipation.
- **Additional adverse experiences occurring in less than 1%** of patients or subjects who received Lansoprazole in trials are shown below:
- **Body as a Whole**: abdomen enlarged, allergic reaction, asthenia, back pain, candidiasis, carcinoma, chest pain (not otherwise specified), chills, edema, fever, flu syndrome, halitosis, infection (not otherwise specified), malaise, neck pain, neck rigidity, pain, pelvic pain.
- **Cardiovascular System**: angina, arrhythmia, bradycardia, cerebrovascular accident/cerebral infarction, hypertension/hypotension, migraine, myocardial infarction, palpitations, shock (circulatory failure), syncope, tachycardia, vasodilation
- **Digestive System**: abnormal stools, anorexia, bezoar, cardiospasm, cholelithiasis, colitis, dry mouth, dyspepsia, dysphagia, enteritis, eructation, esophageal stenosis, esophageal ulcer, esophagitis, fecal discoloration, Flatulence, gastric nodules/fundic gland polyps, gastritis, gastroenteritis, gastrointestinal anomaly, gastrointestinal disorder, gastrointestinal hemorrhage, glossitis, gum hemorrhage, hematemesis, increased appetite, increased salivation, melena, mouth ulceration, nausea and vomiting, nausea and vomiting and diarrhea, gastrointestinal moniliasis, rectal disorder, rectal hemorrhage, stomatitis, tenesmus, thirst, tongue disorder, ulcerative colitis, ulcerative stomatitis
- **Endocrine System:** diabetes mellitus, goiter, hypothyroidism
- **Hemic and Lymphatic System:** anemia, hemolysis, lymphadenopathy
- **Metabolism and Nutritional Disorders:** avitaminosis, gout, dehydration, hyperglycemia/ hypoglycemia, peripheral edema, weight gain/loss
- **Musculoskeletal System:** arthralgia, arthritis, bone disorder, joint disorder, leg cramps, musculoskeletal pain, myalgia, myasthenia, ptosis, synovitis
- **Nervous System:** abnormal dreams, agitation, amnesia, anxiety, apathy, confusion, convulsion, dementia, depersonalization, depression, diplopia, dizziness, emotional lability, hallucinations, hemiplegia, hostility aggravated, hyperkinesia, hypertonia, hypesthesia, insomnia, libido decreased/increased, nervousness, neurosis, paresthesia, sleep disorder, somnolence, thinking abnormality, tremor, vertigo
- **Respiratory System:** asthma, bronchitis, cough increased, dyspnea, epistaxis, hemoptysis, hiccup, laryngeal neoplasia, lung fibrosis, pharyngitis, pleural disorder, pneumonia, respiratory disorder, upper respiratory inflammation/infection, rhinitis, sinusitis, stridor.

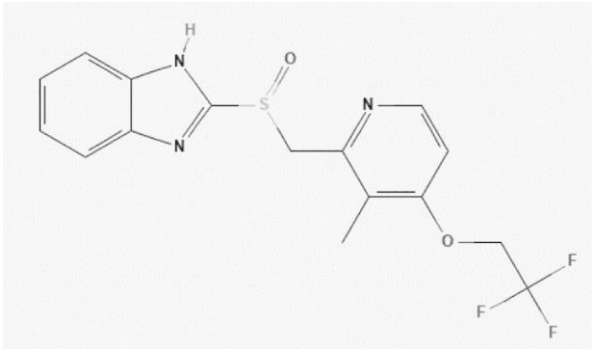
- **Skin and Appendages**: acne, alopecia, contact dermatitis, dry skin, fixed eruption, hair disorder, maculopapular rash, nail disorder, pruritus, rash, skin carcinoma, skin disorder, sweating, urticaria.

4.9. Overdose

Initiate general symptomatic and supportive measures in all cases of overdosages where necessary.

5. Pharmacological properties

The active ingredient in Lanrief Orally Disintegrating Tablets is lansoprazole, a substituted benzimidazole, 2-[[3-methyl-4-(2,2,2-trifluoroethoxy) pyridin-2-yl] methyl sulfinyl]-1H-benzimidazole, a compound that inhibits gastric acid secretion. Its empirical formula is $C_{16}H_{14}F_3N_3O_2S$ with a molecular weight of 369.4 g/mol. Lansoprazole has the following structure:



5.1. Mechanism of action

Lanrief (lansoprazole) belongs to a class of antisecretory compounds, the substituted benzimidazoles, 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.

5.2. Pharmacodynamic properties

In paediatric patients who received lansoprazole daily for 5 days, the mean gastric pH increased from pH 2.5 (baseline) to pH 3.6 with lansoprazole (15 mg) and from pH 2.3 to 3.8 with lansoprazole (30 mg). In children < 30 kg, lansoprazole (15 mg) maintained a gastric pH > 3 - 4 on day 5 for 23 - 54% of the time compared to 12 - 41% prior to lansoprazole therapy. In paediatric patients > 30 kg who received lansoprazole (30 mg/day), the percentage of time the gastric pH > 3 - 4 was increased from 20 - 60%, compared to 9 - 49% prior to treatment, respectively.

Serum gastrin concentration increases with PPI therapy. Suppression of gastric acid secretion stimulates the release of gastrin, a polypeptide hormone secreted by antral G cells in the stomach. Patients with duodenal or gastric ulcers treated with lansoprazole (30 mg/day) for 8 weeks experienced an increase in mean serum gastrin concentration to 286 ng/ml from 118 ng/ml prior to treatment. The mean serum gastrin level remained elevated at 185 ng/ml in patients who received maintenance therapy with H_2- receptor antagonists but returned to normal in patients who did not require antisecretory therapy. Phase II studies of lansoprazole in paediatric subjects aged 1 - 11 years yielded similar results, with an increase in the median serum gastrin concentration from 50 to 100 ng/ml after 8 - 12 weeks of lansoprazole (15 mg daily) and from 52 to 91 ng/ml with lansoprazole (30 mg daily). H. pylori infection is also associated with hypergastrinaemia. Eradication of H. pylori infection was reported to minimise the increase in serum gastrin concentration during omeprazole therapy compared to the rise in gastrin levels observed in patients in whom H. pylori was not eradicated. Morphological changes in gastric mucosa occur in experimental animals receiving long-term therapy with high doses of lansoprazole. Hypertrophy of the parietal cells and gastric glands occurred in rats given lansoprazole 50 mg/kg/day for 1 year. Hypergastrinaemia induced gastric enterochromaffin-like (ECL) cell hyperplasia and ECL carcinoids in some animal models. However, no significant increase in ECL density was observed in humans in one study with long-term use of up to 5.5 years. Another study identified H. pylori infection as a risk factor for argyrophil cell hyperplasia in patients who received lansoprazole for 5 years.

5.3. Pharmacokinetic properties

Lansoprazole is rapidly absorbed after oral doses, with peak plasma concentrations achieved after about 1.5 to 2 hours. Bioavailability is reported to be 80% or more even with the first dose, 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%. It is extensively metabolised in the liver, primarily by cytochrome P450 isoenzyme CYP2C19 to form 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 urine. The plasma elimination half-life is around 1 to 2 hours, but the duration of action is much longer. Lansoprazole is about 97% bound to plasma protein. Clearance is decreased in elderly patients, and in hepatic impairment.

6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology: Not required.

7. Description

Already mentioned and covered in the above points.

8. Pharmaceutical particulars

8.1 Incompatibilities

There are no known incompatibilities.

8.2 Shelf-life: 24 months

8.3 Packaging Information

Lanrief orally disintegrating tablets 15mg/30mg, 10 tablets per strip

8.4 Storage and handling instructions

Store below 30 ^{0}C. Protect from light and moisture. Keep all medicine out of reach of children.

9. Patient Counselling Information

9.1 Adverse reactions: Refer part 4.8.

9.2 Drug Interactions: Refer part 4.5.

9.3 Dosage: Refer part 4.2.

9.4 Storage: Refer part 8.4.

9.5 Risk factors: Refer part 4.4.

9.6 Self-monitoring information: NA

9.7 Information on when to contact a health care provider or seek emergency help.

Patient is advised to be alert for the emergence or worsening of the adverse reactions and contact the prescribing physician.

9.8 Contraindications: Refer part 4.3.

10. Details of manufacturer:

Ravenbhel Healthcare Pvt.Ltd.

(WHO & cGMP Certified Company)

16-17, EPIP, SIDCO, Kartholi, Bari Brahmana, Jammu-181133

11. Details of permission or license number with date: Mfg.Lic.No.: JK/01/56

12. Date of revision: October 2024