SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of Medicinal Product

LANPRACID 15

INN: Lansoprazole Delayed Release Capsules USP 15 mg

2. Qualitative and Quantitative Composition

Each hard gelatin capsule contains:

Lansoprazole USP
(as enteric coated pellets) ……..15 mg

3. Pharmaceutical Particulars

Oral Capsules

Hard gelatin capsules size "2" having Red colour, cap and white colour body containing white coloured spherical pellets.

4. Clinical Particulars

4.1 Therapeutic Indications

Lansoprazole is effective in the treatment of acid-related disorders of the upper gastro-intestinal tract:

- Duodenal ulcer.
- Benign gastric ulcer
- Oesophagitis related to Gastro Oesophageal Reflux.
- Symptomatic Gastro oesophageal Reflux.
- Treatment and prophylaxis of NSAID-associated benign gastric ulcers, duodenal ulcers in patients requiring continued NSAID treatment.
- Helicobacter pylori eradication with concomitant administration of adequate antibiotic, in patient with Helicobacter pylori-related ulcer.
- Long term management of pathological hypersecretory conditions including Zollinger-Ellison syndrome.

4.2 Posology and Method of administration:

- Duodenal ulcer and benign gastric ulcer: Lansoprazole 30 mg once daily for 4 weeks. For prevention of relapse, the recommended maintenance dose is Lansoprazole 15 mg once daily. For those patients not fully healed at this time, a further 4 weeks treatment at the same dosage should be given.
- 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.
- *Helicobacter pylori* eradication with concomitant administration of adequate antibiotic, in patient with Helicobacter pylori-related ulcer: Lansoprazole 30 mg twice daily for 7 days, concomitantly with antibitherapy (amoxicillin, clarithromycin). Treatment may be prolonged up to 14 days, depending on the response.
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- Esophagitis related to Gastro Oesophageal Reflux: Lansoprazole 30 mg once daily for 4 weeks. The majority of patients will be healed after the first course. For those patients not fully healed at this time, a further 4 weeks treatment at the same dosage should be given.
- Symptomatic Gastro Oesophageal Reflux: The recommended dosage is Lansoprazole 15 mg or 30 mg once daily for 2-4 weeks depending on the severity and persistence of symptoms. Patients who do not respond after 4 weeks, or who relapse shortly afterwards, should be investigated.
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- Prohylaxis of NSAID-associated gastric and duodenal ulcer in patients at risk (older patient with history of gastric or duodenal ulcer) on long-term NSAID treatment:

  15 mg once daily. If the treatment fails, the dose 30 mg once daily should be used.

- Long term management of pathological hypersecretory conditions including Zollinger-Ellison syndrome: The initial dose should be 60 mg once daily. The dosage should then be adjusted individually. Treatment should be continued for as long as clinically indicated.

For patients who require 120 mg or more per day, the dose should be divided and administered twice daily.

To achieve the optimal acid inhibitory effect, and hence most rapid healing and symptom relief, lansoprazole 'once daily' should be administered in the morning before food. Lansoprazole 'twice daily' should be administered once in the morning before food, and once in the evening. Do not crush or chew the capsules. The capsules should be swallowed whole before a meal.

- Elderly: Dose adjustment is not required in the elderly. The maximal daily dosage should not exceed 30 mg.
- Children: There is no experience with lansoprazole capsules in children.
- Impaired Hepatic and Renal Function: There is no need to alter the dosage in patients with impaired renal function. Patients with mild to moderate impairment of hepatic function should be kept under regular supervision, and the daily dose should be reduced by 50%.
- 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. Impaired hepatic or renal function: There is no need for a dose adjustment in patients with impaired renal function. Patients with moderate or severe liver disease should be kept under regular supervision and a 50% reduction of the daily dose is recommended.

Method of administration

Lansoprazole should be taken at least 30 minutes before food. Capsules should be swallowed whole with liquid.

4.3.Contraindications

- Hypersensitivity to lansoprazole or to any of the ingredients.

- Pregnancy and lactation.
- Liver impairment.

4.4. Special Warning and Precautions for use:

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 Lansoprazole 15 mg Gastro-Resistant Capsules. SCLE after previous treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.

4.5. Pregnancy and Lactation

Pregnancy:

For lansoprazole no clinical data on exposed pregnancies are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.

Therefore, the use of lansoprazole during pregnancy is not recommended.

Breastfeeding:

It is not known whether lansoprazole is excreted in human breast milk. Animal studies have shown excretion of lansoprazole in 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.

4.6. Interaction with other medicinal products and other forms of interaction

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: A study has shown that 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 Cmax). 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.

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*. The clinical relevance of this is unknown.

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.

4.7. 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.

4.8. Secondary effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

The following side effects are common (may affect up to 1 in 10 people):

• headache, dizziness • diarrhoea, constipation, stomach pains, feeling or being sick, wind, dry or sore mouth or throat • skin rash, itching • changes in liver function test values • tiredness • benign polyps in the stomach.

The following side effects are uncommon (may affect up to 1 in 100 people):

• depression • joint or muscle pain • fluid retention or swelling • changes in blood cell counts • fracture of the hip, wrist or spine

The following side effects are rare (may affect up to 1 in 1,000 people):

• fever • restlessness, drowsiness, confusion, hallucinations, insomnia, visual disturbances, vertigo • a change in the way things taste, loss of appetite, inflammation of your tongue (glossitis) • skin reactions such as burning or pricking feeling under the skin, bruising, reddening and excessive sweating • sensitivity to light • hair loss • feelings of ants creeping over the skin (paresthesiae), trembling • anaemia (paleness) • kidney problems • pancreatitis • inflammation of the liver (may be seen as yellow skin or eyes) • breast swelling in males, impotence • candidiasis (fungal infection, may affect skin or the mucosa) • angioedema; You should see your doctor immediately if you experience symptoms of angioedema, such as swollen face, tongue or pharynx, difficulty to swallow, hives and difficulties to breathe.

The following side effects are very rare (may affect up to 1 in 10,000 people):

• severe hypersensitivity reactions including shock. Symptoms of a hypersensitivity reaction may include fever, rash, swelling and sometimes a fall in blood pressure • inflammation of your mouth (stomatitis) • colitis (bowel inflammation) • changes in test values such as sodium, cholesterol and triglyceride levels • very severe skin reactions with reddening, blistering, severe inflammation and skin loss. (StevensJohnson syndrome, toxic epidermal necrolysis) • very rarely Lansoprazole may cause a reduction in the number of white blood cells and your resistance to infection may be decreased. If you experience an infection with symptoms such as fever and serious deterioration of your general condition, or fever with local infection symptoms such as sore throat/pharynx/mouth or urinary problems you should see your doctor immediately. A blood test will be taken to check possible reduction of white blood cells (agranulocytosis).

Frequency not known (frequency cannot be estimated from the available data)

• If you are on Lansoprazole for more than three months it is possible that the levels of magnesium in your blood may fall. Low levels of magnesium can be seen as fatigue, involuntary muscle contractions, disorentation, convulsions, dizziness, increased heart rate. If you get any of these symptoms, please tell your doctor promptly. Low levels of magnesium can also lead to a reduction in potassium or calcium levels in the blood. Your doctor may decide to perform regular blood tests to monitor your levels of magnesium. • rash, possibly with pain in the joints. • visual hallucinations.

4.9. Overdose

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.

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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Lansoprazole is a member of a class of drugs called proton pump inhibitors. Its mode of action is to inhibit specifically the H+/K+ ATPase (proton pump) of the parietal cell in the stomach, the terminal step in acid production, thus reducing gastric acidity, a key requirement for healing of acid-related disorders such as gastric ulcer, duodenal ulcer and reflux oesophagitis. A single dose of 30 mg inhibits pentagastrin-stimulated acid secretion by approximately 80%, indicating effective acid inhibition from the first day of dosing. Lansoprazole has a prolonged pharmacological action providing effective acid suppression over 24 hours, thereby promoting rapid healing and symptom relief. By reducing gastric acidity, Lansoprazole creates an environment in which appropriate antibiotics can be effective against Helicobacter pylori. In vitro studies have shown that lansoprazole has a direct antimicrobial effect on Helicobacter pylori.

5.2. Pharmacokinetic properties

Lansoprazole is metabolised substantially by the liver. Lansoprazole exhibits high (80-90%) bioavailability with a single dose. As a result, effective acid inhibition is achieved rapidly. Peak plasma levels occurred within 1.5 to 2.0 hours. The plasma elimination half-life ranges from 1 to 2 hours following single or multiple doses in healthy subjects. There is no evidence of accumulation following multiple doses in healthy subjects. The plasma protein binding is 97%. Lansoprazole is extensively metabolised in the liver, and its metabolites are excreted by both the renal and biliary route. A study with 14C-labelled lansoprazole indicated that up to 50% of the dose was excreted in the urine. Preclinical safety data Preclinical data reveal no special hazards for humans based on conventional studies of safety pharmacology, repeated dose toxicity, toxicity to reproduction or genotoxicity. In two rat carcinogenicity studies, lansoprazole produced dose-related gastric ECL cell hyperplasia and ECL cell carcinoids associated with hypergastrinaemia due to inhibition of acid secretion. Intestinal metaplasia was also observed, as were Leydig cell hyperplasia and benign Leydig cell tumours. After 18 months of treatment retinal atrophy was observed. This was not seen in monkeys, dogs or mice. In mouse carcinogenicity studies dose-related gastric ECL cell hyperplasia developed as well as liver tumours and adenoma of rete testis. The clinical relevance of these findings is unknown.

Lansoprazole is a racemate of two active enantiomers that are biotransformed into the active form in the acidic environment of the parietal cells. As lansoprazole is rapidly inactivated by gastric acid, it is administered orally in enteric-coated form(s) for systemic absorption.

Absorption and distribution

Lansoprazole exhibits high (80-90%) bioavailability with a single dose. Peak plasma levels occur within 1.5 to 2.0 hours. Intake of food slows the absorption rate of lansoprazole and reduces the bioavailability by about 50%. The plasma protein binding is 97%.

Studies have shown that granules from opened capsules give equivalent AUC as the intact capsule if the granules are suspended in a small amount of orange juice, apple juice, or tomato juice mixed with a tablespoon of apple or pear puree or sprinkled on a tablespoon of yoghurt, pudding or cottage cheese. Equivalent AUC has also been shown for granules suspended in apple juice administered through a naso-gastric tube.

Metabolism and elimination

Lansoprazole is extensively metabolised by the liver and the metabolites are excreted by both the renal and biliary route. The metabolism of lansoprazole is mainly catalysed by the enzyme CYP2C19. The enzyme CYP3A4 also contributes to the metabolism. The plasma elimination half-life ranges from 1 to 2 hours following single or multiple doses in healthy subjects. There is no evidence of accumulation following multiple doses in healthy subjects. Sulphone, sulphide and 5-hydroxyl derivatives of lansoprazole have been identified in plasma. These metabolites have very little or no antisecretory activity.

A study with 14C labelled lansoprazole indicated that approximately one-third of the administered radiation was excreted in the urine and two-thirds was recovered in the faeces.

Pharmacokinetics in elderly patients

The clearance of lansoprazole is decreased in the elderly, with elimination half-life increased approximately 50% to 100%. Peak plasma levels were not increased in the elderly. Pharmacokinetics in paediatric patients The evaluation of the pharmacokinetics in children aged 1 –17 years of age showed a similar exposure as compared to adults with doses of 15 mg for

those below 30 kg of weight and 30 mg for those above. The investigation of a dose of 17 mg/m2 body surface or 1 mg/kg body weight also resulted in comparable exposure of lansoprazole in children aged 2-3 months up to one year of age compared to adults.

Higher exposure to lansoprazole in comparison to adults has been seen in infants below the age of 2-3 months with doses of both 1.0 mg/kg and 0.5 mg/kg body weight given as a single dose. Pharmacokinetics in hepatic insufficiency

The exposure of lansoprazole is doubled in patients with mild hepatic impairment and much more increased in patients with moderate and severe hepatic impairment.

CYP2C19 is subject to genetic polymorphism and 2-6 % of the population, called poor metabolisers (PMs), are homozygote for a mutant CYP2C19 allele and therefore lacks a functional CYP2C19 enzyme. The exposure of lansoprazole is several-fold higher in PMs than in extensive metabolisers (EMs).

5.3. Preclinical safety data

20Preclinical data reveal no special hazards for humans based on conventional studies of safety pharmacology, repeated dose toxicity, toxicity to reproduction or genotoxicity. In two rat carcinogenicity studies, lansoprazole produced dose-related gastric ECL cell hyperplasia and ECL cell carcinoids associated with hypergastrinaemia due to inhibition of acid secretion. Intestinal metaplasia was also observed, as were Leydig cell hyperplasia and benign Leydig cell tumours. After 18 months of treatment retinal atrophy was observed. This was not seen in monkeys, dogs or mice. In mouse carcinogenicity studies dose-related gastric ECL cellhyperplasia developed as well as liver tumours and adenoma of rete testis. The clinical relevance of these findings is unknown.

6. PHARMACEUTICAL PARTICULARS

6.1.List of Excipients

Non Pareil seeds (Dummy Pellets) (142 – 18#); Empty hard gelatin capsule size “2” with red colour cap & white coloured body

6.2. Incompatibilities

None Known

6.3. Shelf Life

30 months from the date of manufacture.

6.4. Special precautions for Storage

Protect from light. Do not store above 30 ^{o}C.Keep out of the reach of children

6.5. Nature and content of Container

3 x10 Capsules in ALU-ALU Blister pack.

6.6. Special precaution for disposal and other handling

No Special Requirements

7. NAME AND ADDRESS OF MANUFACTURER:

BDA HEALTHCARE PVT. LTD.,
Plot No.: B-1, 2, 3, Near Gov. ITI MIDC, Parseoni – 441105,
Taluka: Parseoni, District: Nagpur, M.S., India.

8. MARKETING AUTHORISATION NUMBER(S)

06432/08088/NMR/2020

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

26.07.2021

10. DATE OF REVISION OF THE TEXT

02 July 2023