1. **NAME OF THE MEDICINAL PRODUCT**

   Lansoprazole 15, gastro-resistant capsule of 15 mg  
   Lansoprazole 30, gastro-resistant capsule of 30 mg

2. **QUALITATIVE AND QUANTITATIVE COMPOSITION**

   Lansoprazole 15 contains 15 mg of lansoprazole per capsule.  
   Lansoprazole 30 contains 30 mg of lansoprazole per capsule.  

   For excipients see section 6.1

3. **PHARMACEUTICAL FORM**

   Gastro-resistant capsule, hard

4. **CLINICAL PARTICULARS**

4.1 **Therapeutic indications**

   Lansoprazole is used in the treatment of patients with an ulcer duodeni, ulcer ventriculi, reflux oesophagitis or Zollinger-Ellison syndrome.

   In combination with two suitable antibiotics (see 4.2. 'Posology and method of administration') for the eradication of Helicobacter pylori in patients with peptic ulcers with the objective to reduce the risk of recurrent ulcer duodeni and ulcer ventriculi, caused by this micro-organism.

4.2 **Posology and method of administration**

   **Posology:**

   *Ulcus duodeni:*
   The recommended dose is 30 mg of lansoprazole once per day. In most patients healing occurs within two weeks.  
   If this treatment is not sufficient, healing is usually reached with the continuation of this treatment for yet another period of 2 weeks.
In special cases a higher dose may be administered if needed, that means up to 60 mg of lansoprazole per day. For instance, this is the case in patients who do not react to other medical treatments.

For maintenance treatment, for the prevention of recurrences, 15 mg of lansoprazole once daily is recommended. If a recurrence does occur during this maintenance treatment anyway, the dose can temporarily be increased to 30 mg once daily.

*Ulcus ventriculi:*
The recommended dose is 30 mg of lansoprazole once per day for a period of four weeks. If this treatment is not sufficient, healing is usually reached with the continuation of this treatment for yet another period of 4 weeks.

In special cases a higher dose may be administered if needed, that means up to 60 mg of lansoprazole per day. For instance, this is the case in patients who do not react to other medical treatments.

*Reflux oesophagitis:*
The recommended dose is 30 mg of lansoprazole once per day for a period of four weeks. If this treatment is not sufficient, healing is usually reached with the continuation of this treatment for yet another period of 4 weeks.

In special cases a higher dose may be administered if needed, that means up to 60 mg of lansoprazole per day. For instance, this is the case in patients who do not react to other medical treatments.

For maintenance treatment, for the prevention of recurrences, 15 mg of lansoprazole once daily is recommended. If a recurrence does occur during this maintenance treatment anyway, the dose can temporarily be increased to 30 mg once daily.

*Zollinger-Ellison syndroom*
The recommended starting dose is 60 mg of lansoprazole once per day. The dose may be adjusted to the individual patient on the basis of the clinical picture. Doses to 90 mg two times daily have been administered to these patients. A dose higher than 120 mg per day should be taken divided over the day.

*Eradication of H. pylori*
The recommended dose is 30 mg of lansoprazole two times daily for seven days together with one of the combinations mentioned below:
- amoxicillin 1 gram two times daily + clarithromycin 500 mg two times daily or
- clarithromycin 500 mg two times daily + metronidazole 500 mg two times daily.

*Children:*
There is still insufficient data regarding the administration of lansoprazole in children.
Elderly patients:
The dose of 30 mg per day should not be exceeded.

Patients with renal insufficiency:
The dose of 30 mg per day should not be exceeded.

Patients with hepatic insufficiency:
The dose is generally 15 mg per day. Do not exceed a dose of 30 mg per day.

Method of administration
Do not chew or crush the capsules. Take with some water, before or after the meal.

4.3 Contraindications
A known hypersensitivity to lansoprazole.

4.4 Special warnings and special precautions for use
In case of ulcer ventriculi the possibility of a malignant disorder should be ruled out; the administration of lansoprazole may mask the malignancy.

In patients with gastro-duodenal ulcer suffering the possibility of an H. pylori infection as an aetiological factor should be taken into account.

If lansoprazole, combined with antibiotics, is administered for the eradication of H. pylori the instructions for the use of these antibiotics should also be adhered to (see also under 4.2.).

If with long-term use (> 1 year) ocular complaints occur, consulting an eye specialist is advised.

This medicinal product contains sucrose. Patients with the rare, hereditary disorder of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not use this medicinal product.

4.5 Interaction with other medicinal products and other forms of interaction
Caution is needed with the concomitant use of substances that are converted in the liver via cytochrome P-450, for instance phenytoin.
Pharmacokinetic interaction studies with the concomitant administration of lansoprazole and the relevant antibiotics amoxicillin and clarithromycin have been done in humans. No clinically relevant interactions were observed.

With the concomitant administration of amoxicillin and clarithromycin and lansoprazole a 30% increase in the AUC of lansoprazole occurs. This increase with the administration of the combination with amoxicillin or clarithromycin has no negative clinical effects for the eradication therapy of the H. pylori infection.

Metronidazole is an inhibitor of the cytochrome P450 3A4. As lansoprazole is a substrate of this isoenzyme, the plasma concentrations of lansoprazole may be elevated when this is administered concomitantly with metronidazole. The interactions of lansoprazole and metronidazole have, however, not been studied well and have also not been reported.

In general no interaction between theophylline and lansoprazole is observed. However, in some people the theophylline clearance may be strongly increased during a treatment with lansoprazole. This should be taken into account. A study with warfarin, an anticoagulant of the coumarin-type, showed that a clinically relevant interaction did not occur.

In healthy volunteers lansoprazole has no effect on the pharmacokinetics of diazepam. The concomitant use of antacids shows a reduction in the bioavailability of lansoprazole. Therefore it is recommended, with a combination of lansoprazole and antacids, not to take these products at the same time but to take them with an interval of at least 1 hour. Concomitant use of lansoprazole and food reduces the bioavailability; therefore lansoprazole should be taken at least a half hour before or after the meal. The bioavailability of lansoprazole is significantly higher in the morning than in the evening. Therefore in the morning lansoprazole should be taken at least a half hour before or after breakfast. Treatment with lansoprazole may affect the bioavailability of medicinal products of which the absorption is dependent on the pH in the stomach.

### 4.6 Pregnancy and lactation

There is insufficient data available about the use of this substance during human pregnancy to determine its toxicity. In experiments with rats placenta crossing of lansoprazole has been shown; concentrations of both the lansoprazole and the metabolites were higher in the plasma of the foetus than in the plasma of the mother. So far there have not been any indications of toxicity in animal tests. Use only during pregnancy after consulting with the treating physician.

In rats the excretion of both lansoprazole and metabolites has been observed in the milk of the mother. At the moment there is no known data about the presence of lansoprazole in human breast milk.
4.7 Effects on ability to drive and use machines

There is no known data about the effect on the ability to drive and use machines. The possibility of dizziness, which may occur incidentally, should be taken into account.

4.8 Undesirable effects

A few times the following symptoms were observed:

**Blood and lymphatic system disorders:**
agranulocytosis, thrombocytopenia, anaemia, leucopenia, and eosinophilia have been reported sporadically.

**Nervous system disorders:**
in a few cases dizziness, headache, sleepiness, insomnia was reported.

**Gastrointestinal disorders:**
diarrhoea, constipation, nausea/vomiting, abdominal pain, dry mouth. Also a few cases of colitis have been reported.

**Hepato-biliary disorders:**
Reversible increase of transaminases, alkaline phosphatase, gamma-glutamyl transpeptidase and bilirubin. In rare cases laboratory values can be measured up to more than twice the normal values, which can indicate liver damage.
Rare: hepatitis

**Skin and subcutaneous tissue disorders:**
Stevens-Johnson Syndrome, toxic epidermal necrolysis, exfoliative dermatitis, vesiculobular skin rash, skin reactions, urticaria and itch have been reported.

**Musculoskeletal and connective tissue disorders:**
Muscle aches and joint pain.

**General disorders and administration site conditions:**
anaphylactic reactions, malaise, fever, peripheral oedema.

The symptoms are mild in nature and only rarely a reason to discontinue the therapy.

4.9 Overdose

With an overdose the treatment is dependent of the symptoms that occur. There is no known specific treatment method. Haemodialysis is not meaningful.
5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC-Code: A02B C03

Pharmacotherapeutic group: proton pump inhibitors.

Lansoprazole is a benzimidazole derivative that inhibits the gastric acid producing enzyme (H⁺, K⁺, ATPase) in the parietal cell. Thanks to the inhibition of the last stage in the acid production both the basal and the stimulated acid secretion in the stomach are inhibited. This rapid and effective inhibition is dose dependent and reversible. The lansoprazole has no effect on the histamine receptors and acetyl choline receptors. Two hours after a single administration of 30 mg of lansoprazole the acid production in the stomach is reduced by approximately 80%.

With continued treatment an oral administration of 30 mg of lansoprazole once daily provides a reduction of the basal acid secretion of 72% the first day increasing to 87% on the eighth day of the treatment.

The maximum of the acid production, stimulated with pentagastrin, is inhibited by lansoprazole from 81 % increasing to 90% in the same period of time.

5.2 Pharmacokinetic properties

Absorption:
Lansoprazole is administered in gastric acid resistant granules in a capsule. After passage from the stomach the absorption of lansoprazole is rapid and the maximum plasma concentration is reached 1 to 3 hours after intake. With concomitant use of food the bioavailability is reduced considerably.

Distribution:
Lansoprazole is primarily distributed across the extra-cellular fluid. The distribution volume is on average 29 litres. The protein binding is about 97%.

Metabolism and excretion:
The data below concerns studies in healthy volunteers. The plasma-elimination half life is approximately 1.4 hours. During the treatment accumulation does not occur. Lansoprazole is primarily converted into inactive metabolites in the liver.

Lansoprazole is largely eliminated via de liver. 15 to 30% of the administered dose is excreted in the urine in the form of metabolites.
In elderly patients the pharmacokinetic profile of lansoprazole is not significantly different from that of young adults.

With renal insufficiency the pharmacokinetics does not change in such a way that dose adjustment is needed.

With hepatic insufficiency the maximum plasma levels, the terminal plasma half life and thus the area under the curve (AUC) increase significantly. In this case a maximum dose of 30 mg should not be exceeded.

5.3 **Preclinical safety data**

In test animals toxicity is primarily observed in the stomach. There is a clear trend that this toxicity occurs at continuously lower doses with prolonged treatment duration. The margin between safe and toxic doses becomes therefore smaller with long-term treatment. The relevance of the gastric changes for humans is unclear. In the rat ocular disorders (retinal atrophy and cataract) are observed after the long-term administration of lansoprazole. The underlying mechanism is not known. Specialised studies in humans after the use of a dose of 15 to 180 mg per day for 1 year has not provided any indications of toxicity so far, but the extent of the studied population is limited.

6. **PHARMACEUTICAL PARTICULARS**

6.1 **List of excipients**

Saccharose  
Maize starch  
Hypropemlose (E 464)  
Talc (E 553b)  
Titanium dioxide (E 171)  
Magnesium carbonate (E 504)  
Methacrylic acid – ethylcrylate copolymer (1:1) dispersion 30%  
Macrogol 400  
Colloidal silicon (water free) (E 551).

Capsule shell:  
Carrageen (E 407)  
Potassium chloride (E 508)  
Titanium dioxide (E 171)  
Hypropemlose (E 464)
6.2 Incompatibilities

No known incompatibilities.

6.3 Shelf life

18 months.

6.3 Special precautions for storage

Do not store above 25°C.
Store in the original package.

6.4 Nature and contents of container

Lansoprazole 15/30: 7, 10, 14, 15, 20, 21, 28, 30, 56, 84, 98, 100 and 100x1 in blister pack (Al/Al).

6.5 Instructions for use and handling

No particulars.

7. MARKETING AUTHORISATION HOLDER

Stichting Registratiebeheer
Bosstraat 69
3766 AC Soest

8. MARKETING AUTHORISATION NUMBER(S)

Lansoprazole 15 is registered under number: RVG 31123
Lansoprazole 30 is registered under number: RVG 31124

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT