

ANNEX I

**LIST OF THE NAMES, PHARMACEUTICAL FORM, STRENGTHS OF THE MEDICINAL
PRODUCTS, ROUTE OF ADMINISTRATION, APPLICANT, MARKETING
AUTHORISATION HOLDER IN THE MEMBER STATES**

<u>Member State</u>	<u>Marketing Authorisation Holder</u>	<u>Applicant</u>	<u>Invented name</u>	<u>Strength</u>	<u>Pharmaceutical Form</u>	<u>Route of administration</u>
Finland	ratiopharm GmbH Graf-Arco-Str. 3 89075 Ulm Germany	-	Lansoprazol AbZ-Pharma 15 mg	15 mg	Gastro-resistant capsule, hard	Oral use
			Lansoprazol AbZ-Pharma 30 mg	30 mg	Gastro-resistant capsule, hard	Oral use
Germany	-	ratiopharm GmbH Graf-Arco-Str. 3 89075 Ulm Germany	Lansoprazol AbZ 15 mg Hartkapseln	15 mg	Gastro-resistant capsule, hard	Oral use
			Lansoprazol AbZ 30 mg Hartkapseln	30 mg	Gastro-resistant capsule, hard	Oral use

ANNEX II

**SCIENTIFIC CONCLUSIONS AND GROUNDS FOR AMENDMENT OF THE SUMMARY
OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLET
PRESENTED BY THE EMEA**

SCIENTIFIC CONCLUSIONS

OVERALL SUMMARY OF THE SCIENTIFIC EVALUATION OF LANSOPRAZOL ABZ-PHARMA 15 MG, 30 MG, GASTRO-RESISTANT CAPSULES, HARD (see Annex I)

Lansoprazol AbZ-Pharma 15 mg, 30 mg, gastro-resistant capsules, hard were referred for arbitration according to Article 29 of Council Directive 2001/83/EC, as amended, following concerns raised by Germany during a Mutual Recognition Procedure with Finland acting as Reference Member state. The concerns rose referred to discrepancies in comparison to the reference products on posology of triple therapy for *H. pylori* eradication.

Eradication of *H. pylori* and peptic ulcer healing

In order to standardise the treatment regimens for *H. pylori* eradication guidelines on the management of *Helicobacter pylori* infection were published by the European *Helicobacter pylori* Study Group. The Maastricht Consensus stated that treatment regimens for eradication of *H. pylori* should be simple, well tolerated and achieve an eradication rate of over 80% on an intention to treat basis.

The treatment regimens that have been shown to satisfy the criteria required above were following:

Standard dose proton pump inhibitor, twice daily, and:

- metronidazole, 400 mg (tinidazole, 500 mg) twice daily, + clarithromycin, 250 mg twice daily;
- amoxicillin, 1000 mg twice daily, + clarithromycin, 500 mg twice daily (advisable when metronidazole resistance is likely);
- amoxicillin, 500 mg three times daily, + metronidazole, 400 mg three times daily (advisable when clarithromycin resistance is likely)

Since then new data became available that necessitated an update of the original guidelines in order to provide practical management guidelines that would be acceptable across clinical practice, both in primary care and the specialist level. The updated guidelines were established during the Maastricht 2-2000 Consensus meeting. It was pointed out that treatment should be thought of as a package, which considers first- and second-line eradication therapies together. First line therapy should be with triple therapy using a proton pump inhibitor or ranitidine bismuth citrate, combined with clarithromycin (500 mg twice daily) and amoxicillin (1 g twice daily) or metronidazole (500 twice daily).

Metronidazole was originally considered as an alternative to amoxicillin but there is now tendency to reserve it for rescue therapy in the case of a first eradication failure. Second-line therapy with quadruple therapy using proton pump inhibitor combined with bismuth subcitrate (subsalicylate) and metronidazole, and tetracycline for a minimum of 7 days has been recommended. If bismuth is not available, PPI-based triple therapies should be used. Subsequent failures should be handled on case-by-case basis.

Reduction of the clarithromycin dose in the clarithromycin-metronidazole combination is supported by clinical data as well as the Maastricht Consensus Report, stating that 250 mg dose is sufficient even if the recommended dose is 500 mg. The reduction of clarithromycin to 250 mg in the triple combination therapy with amoxicillin 1000 mg, however, is not supported by the Maastricht 2-2000 Consensus Report. The paper newly published by Bago et al in Wiener Klinische Wochenschrift 2004, indicates that 250 mg twice daily may be as effective as 500 mg twice daily in eradicating *H. pylori* in patients with dyspepsia, even if numerically, eradication rates were somewhat lower. However, awaiting confirmation as well as the results of the Maastricht 3-2005 Consensus Report, it is recommended that the dose should be 500 mg clarithromycin twice daily.

Benefit/Risk considerations

Available data support the use of lansoprazole-amoxicillin-clarithromycin as a first-line treatment. In case of clarithromycin resistance, or treatment failure, the combination of lansoprazole-amoxicillin-

metronidazole may be used, and in case of beta-lactam allergy the combination of lansoprazole-clarithromycin-metronidazole is advisable. However, in order to avoid treatment failure, local antibacterial resistance patterns and local guidelines should be considered.

The risk/benefit ratio of Lansoprazol AbZ-Pharma 15 mg, 30 mg is considered to be favourable provided that appropriate information regarding *H. pylori* eradication therapy are included in the SPC.

GROUND FOR AMENDMENT OF THE SUMMARY OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLET

Whereas,

- The scope of the referral was to agree on a harmonised dosing schedule for triple therapy for eradication therapy for *H. pylori*
- The Summary of Products Characteristic, labelling and package leaflet proposed by the applicant has been assessed based on the documentation submitted and the scientific discussion within the Committee.

the CHMP has recommended the granting of the Marketing Authorisations for which the Summary of Product Characteristics, labelling and package leaflet are set out in Annex III for Lansoprazol AbZ-Pharma and associated names (see Annex I).

ANNEX III

SUMMARY OF PRODUCT CHARACTERISTICS, LABELLING AND PACKAGE LEAFLET

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

< Lansoprazol AbZ and associated names (see Annex I) 15 mg , gastro-resistant capsules, hard >

< Lansoprazol AbZ and associated names (see Annex I) 30 mg , gastro-resistant capsules, hard >

[see Annex I – to be completed nationally]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 15 mg or 30 mg lansoprazole.

Also contains sucrose (sugar).

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Gastro-resistant hard capsule.

15 mg:

Opaque yellow cap and body.

30 mg:

Opaque white cap and body.

4. CLINICAL PARTICULARS

4.1 Therapeutical indications

- Treatment of duodenal and gastric ulcer confirmed by endoscopy or radiography
- Treatment of reflux oesophagitis
- Long-term prophylaxis of reflux oesophagitis
- Eradication of *Helicobacter pylori* concurrently given with appropriate antibiotic therapy and prevention of relapse of peptic ulcers in patients with *H. pylori* associated ulcers
- Zollinger-Ellison Syndrome

4.2 Posology and method of administration

Duodenal ulcer:

The recommended dose is 30 mg once daily for 2 weeks. In patients not fully healed within this time, the medication should be continued at the same dose for another 2 weeks.

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 should be continued at the same dose for another 4 weeks.

Reflux oesophagitis:

The recommended dose of lansoprazole 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.

Long-term prophylaxis of reflux oesophagitis:

15 mg once daily. The dose may be increased up to 30 mg daily as necessary.

Helicobacter pylori eradication:

The recommended dose is 30 mg lansoprazole 2 times daily for one week in combination with one of the following three combinations:

- a) amoxicillin 1 g twice daily + clarithromycin 500 mg twice daily,
- b) clarithromycin 250 mg twice daily + metronidazole 400-500 mg twice daily,
- c) amoxicillin 1 g twice daily + metronidazole 400-500 mg twice daily.

Consideration should be given to official local guidance (e.g. national recommendations) regarding bacterial resistance and the appropriate use and prescription of antibacterial agents.

Zollinger-Ellison Syndrome:

The recommended adult oral starting dose is 60 mg once a day. Doses should be adjusted to individual patient needs and should continue for as long as clinically indicated. Dosages up to 180 mg have been administered. Daily dosages of greater than 120 mg should be administered in divided doses.

Patients with renal or hepatic impairment:

Dosage adjustment is not necessary in patients with renal insufficiency. However the normal daily dose of 30 mg should not be exceeded. Care should be exercised in the administration of lansoprazole in patients with mildly to moderately impaired hepatic function. In mildly impaired patients, the dose should not exceed 30 mg. In patients with moderately impaired hepatic function, the dose should be restricted to 15 mg daily. Due to the lack of data in patients with severely impaired hepatic function, these patients should not be treated with lansoprazole.

Combination treatment with clarithromycine should not be used in patients with impaired hepatic function.

Children:

Lansoprazole is not recommended for use in children due to insufficient data on safety and efficacy.

Elderly:

Due to delayed elimination of lansoprazole in the elderly it may be necessary to administer the treatment in doses of 15-30 mg adjusted to individual requirements. However, the daily dose in the elderly should not exceed 30 mg.

The capsules are swallowed whole with liquid. The capsules may be emptied, but the contents may not be chewed or ground. Concomitantly taken food slows down and reduces the absorption of lansoprazole. This medicine has the best effect when taken into empty stomach.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients.

4.4 Special warnings and precautions for use

The diagnosis of gastroduodenal ulcers and reflux oesophagitis should be confirmed by endoscopy or other appropriate diagnostic means. Reflux oesophagitis may not present, as ulceration and/or visual damage, therefore in certain cases endoscopy alone may not be sufficient.

The possibility of malignant gastric tumour should be excluded before initiating treatment of gastric ulcer with lansoprazole because lansoprazole can mask the symptoms and delay the diagnosis.

Lansoprazole should be used with caution in patients with hepatic dysfunction. (See Section 4.2 Posology and Method of Administration)

Lansoprazole has similar mechanism of action to omeprazole and both increase gastric pH, the following statement is made by analogy to omeprazole. Decreased gastric acidity due to lansoprazole increases 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*.

Patients suffering from gastro-duodenal ulcers, the possibility of *H. pylori* infection as an etiological factor should be considered. If lansoprazole, in combination with antibiotics, is used for eradication therapy of *H. pylori*, then also instructions for the use of these antibiotics should 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 benefit risk assessment should regularly be performed in these patients.

If visual disturbances occur during long-term use (>1 year), intake of the medicine should immediately be stopped and an ophthalmologist should be consulted.

Since this product contains sucrose, patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Active substances associated with cytochrome P450

As lansoprazole is metabolised via a drug metabolising enzyme system associated with cytochrome P450 (CYP2C19 and CYP3A4), interactions with active substances metabolised via the same enzyme system are possible.

The effects of other active substances on lansoprazole

Active substances, which inhibit CYP2C19

Active substances, which inhibit CYP2C19 may increase the plasma concentration of lansoprazole. Fluvoxamine, an inhibitor of CYP2C19, increased the plasma concentrations of lansoprazole up to 4-fold.

Active substances, which inhibit CYP3A4

Active substances, which inhibit CYP3A4 such as ketokonazole, itraconazole, protease inhibitors, macrolides etc may markedly increase the plasma concentrations of lansoprazole.

Effects of lansoprazole on other active substances

Ketoconazole and itraconazole

The absorption of ketoconazole and itraconazole from the gastrointestinal tract is enhanced by the presence of gastric acid. This result in sub-therapeutic concentrations of ketoconazole and itraconazole and the combination should be avoided. The effect may also be present if lansoprazole is combined with other active substances with pH dependent absorption.

Digoxin

Coadministration of lansoprazole and digoxin may lead to increased digoxin plasma levels. In patients receiving digoxin, the plasma levels should therefore be monitored and the dose of digoxin adjusted if necessary.

Active substances metabolised by CYP3A4

Lansoprazole may give rise to increased plasma concentrations of active substances metabolised by CYP3A4. Caution is advised when combining lansoprazole with active substances, which are metabolised by this enzyme.

Tacrolimus

Co-administration of lansoprazole increases the plasma concentrations of tacrolimus (a CYP3A and P-gp substrate). Lansoprazole exposure increased the mean exposure of tacrolimus by up to 81%. Monitoring of tacrolimus plasma concentrations is advised when concomitant treatment with lansoprazole is initiated or ended.

Carbamazepine

Caution is advised during co-treatment with carbamazepine (a CYP3A substrate) and lansoprazole. The drug combination may result in increased carbamazepine concentrations as well as reduced lansoprazole concentrations.

Phenytoin

Studies have shown that the dose of phenytoin (a CYP2C19 and CYP2C9 substrate) may have to be reduced when administered concomitantly with lansoprazole. Caution and monitoring of phenytoin plasma concentrations is advised when initiating and ending lansoprazole treatment.

Warfarin

Caution and increased monitoring frequency is advised when initiating or ending lansoprazole co-treatment in patients treated with warfarin.

Theophyllin

Lansoprazole gives a 14% reduction in the plasma concentrations of theophyllin. Individual patients may receive a clinically relevant decrease. Caution is advised when combining the two active substances.

Clinically significant interactions of lansoprazole with diazepam have not been demonstrated. Antacids and sucralfate may decrease the bioavailability of lansoprazole. The Lansoprazole dose should therefore be taken at least an hour prior or after.

Lansoprazole has been observed to inhibit the transport protein, P-glycoprotein (P-gp) *in vitro*. It may not be excluded that lansoprazole may affect transport via this protein giving rise to increased plasma concentrations of P-gp substrates such as digoxin.

Caution should be exercised when combining lansoprazole with active substances which have a narrow therapeutic index, as the effect of lansoprazole on the metabolism of other active substances has not been extensively investigated.

Therapy of *Helicobacter pylori* infection is intended to be combined with concurrent administration of lansoprazole with two antibiotics. The influence of this combined administration has not yet been investigated systemically. For reasons of theoretical considerations, enhanced interactions with other medicinal products must be expected as a precaution. Monitoring of the serum levels of other medicinal products taken during the 1-week eradication therapy is therefore recommended. This concerns particularly such medicinal products also metabolized via the cytochrome P450 system.

The following interactions between lansoprazole and one/two antibiotics used in eradication therapy have been found so far:

Co-administered medicinal products	Dosage and duration of combined administration	<u>Effect*</u>
lansoprazole + clarithromycin	30 mg + 500 mg 3 times/day for 5 days	Increased plasma levels of a clarithromycin metabolite by 16 %; increased bioavailability of lansoprazole by 19 % up to 32 %

lansoprazole + amoxicillin	30 mg + 1000 mg 3 times/day for 5 days	Decelerates uptake of amoxicillin
lansoprazole + metronidazole	Not yet investigated	
lansoprazole + clarithromycin + amoxicillin	30 mg + 500 mg + 1000 mg twice daily for 5 days	Increase bioavailability and half-life of lansoprazole by 30 % each; increased plasma levels of a clarithromycin metabolite by 30 %

* The effects of clarithromycin on the pharmacokinetics of lansoprazole are likely to be dependent on the patient's CYP2C19 genotype. A poor metaboliser would have more marked effects than an extensive metaboliser.

The intake of food reduces the bioavailability of lansoprazole: it is recommended to take lansoprazole before the meal.

4.6 Pregnancy and lactation

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/fetal development, parturition or postnatal development.

The use of lansoprazole during pregnancy is not recommended.

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 breast-feeding to the child and the benefit of lansoprazole therapy to the woman.

4.7 Effects on ability to drive and use machines

Lansoprazol AbZ has minor or moderate influence on the ability to drive and use machines.

4.8 Undesirable effects

The following undesirable effects have been observed during treatment with lansoprazole with the following frequencies: Common (>1/100, <1/10), uncommon (>1/1,000, <1/100), rare (>1/10,000, <1/1,000), very rare (<1/10,000) including isolated reports.

	Common (1/100, <1/10)	Uncommon (>1/1000, <1/100)	Rare (>1/10000, <1/1000)	Very rare (<1/10000) including isolated reports
Gastrointestinal disorders	Vomiting, nausea, diarrhea, stomach ache, constipation, flatulence and dyspepsia.	Dry mouth or throat and anorexia.	Pancreatitis, candidiasis of oesophagus and glossitis.	Colitis, stomatitis and black tongue.
Skin and subcutaneous tissue disorders	Eczema, urticaria and itching.		Erythema multiforme, Petechia, hair loss, hyperhidrosis and purpura .	Stevens-Johnson syndrome and toxic epidermal necrolysis.
Nervous system disorders	Headache and dizziness.		Depression, hallucination, confusion, insomnia, somnolence, drowsiness, vertigo, tremor and paresthesia, restlessness.	
Hepatobiliary disorders		Increase in liver enzyme levels.	Hepatitis and icterus	
Renal and urinary disorders			Interstitial nephritis.	
Blood and lymphatic system disorders			Thrombocytopenia, eosinophilia, pancytopenia, anemia and leucopenia.	Agranulocytosis.
Cardiac disorders			Palpitation and chest pain.	
Vascular disorders			Peripheral edema.	
Musculoskeletal and connective tissue disorders			Muscle and joint pain.	
Eye and taste disorders		Taste disturbances.	Visual disturbances.	
Endocrine disorders				Gynecomastia and galactorrhoea.
General disorders	Fatigue	.	Angioedema, bronchial constriction, fever.	Anaphylactic shock, impotence and general malaise
Investigations				Increase in cholesterol and triglyceride levels.

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

4.9 Overdose

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

Possible symptoms of lansoprazole overdose can be expected to be similar with adverse drug reactions listed in section 4.8.

Lansoprazole is not significantly eliminated by haemodialysis. If necessary, gastric emptying, charcoal and symptomatic therapy is recommended.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Proton pump inhibitors, ATC code: A02BC03.

Lansoprazole is a gastric proton pump inhibitor. It inhibits the final stage of gastric acid formation by inhibiting the activity of H^+/K^+ ATPase of the parietal cells in the stomach. The inhibition is dose-dependent and reversible, and the effect applies to both basal and stimulated secretion of gastric acid. Lansoprazole is concentrated in the parietal cells and becomes active in their acidic environment, whereupon it reacts with the sulphydryl group of H^+/K^+ ATPase causing inhibition of the enzyme activity.

Effect on gastric acid secretion:

Lansoprazole is a specific inhibitor of the parietal cell proton pump. A single oral dose of 30 mg inhibits pentagastrin-stimulated gastric acid secretion by about 80%. After repeated daily administration for seven days, about 90% inhibition of gastric acid secretion is achieved. It has a corresponding effect on the basal secretion of gastric acid. A single oral dose of 30 mg reduces basal secretion by about 70%, and the patients' symptoms are consequently relieved starting from the very first dose. After eight days of repeated administration the reduction is about 85%. A rapid relief of symptoms is obtained by 30 mg daily, and most patients with duodenal ulcer recover within 2 weeks, patients with gastric ulcer and reflux oesophagitis within 4 weeks.

5.2 Pharmacokinetic properties

Absorption and distribution:

Lansoprazole is rapidly inactivated by gastric acid and consequently administered as enteric-coated granules in gelatin capsules. Absorption from the duodenum is rapid and plasma peak concentration is achieved within 1.5-2.0 hours. Bioavailability after a single dose of 30 mg and after repeated daily administration is 80-90%. Intake of food slows the absorption rate of lansoprazole and reduces its bioavailability (AUC) by about 25%. Antacids and sucralfate may reduce the bioavailability of lansoprazole. The plasma protein binding of lansoprazole is about 95%, but this has not been found to have a significant effect on other protein bound active substances.

Metabolism and elimination:

The metabolism of lansoprazole is mainly catalysed by the enzyme CYP2C19. The enzyme CYP3A4 also contributes to the metabolism. 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).

The elimination half-life of lansoprazole is 1.0-2.0 hours. There is no change in half-life during treatment. A single dose of lansoprazole has an inhibitory effect on gastric acid secretion lasting more than 24 hours. Since lansoprazole is activated in the parietal cells, its plasma concentration is not related to gastric acid inhibition. Lansoprazole is mainly metabolised in the liver. Three metabolites

have been identified in the plasma: the sulphone, 5-hydroxy lansoprazole and the sulphide. These metabolites have no significant effect on acid secretion. About 15-50% of the metabolites are secreted in the urine and the remainder in the faeces. Three metabolites have been identified in the urine: 5-hydroxy sulphone, 5-hydroxy sulphide and 5-hydroxy lansoprazole. In patients with cirrhosis the AUC of lansoprazole is significantly increased and the elimination half-life is prolonged, but no signs of accumulation of lansoprazole have been detected. The bioavailability of lansoprazole is not significantly changed in renal insufficiency. Elimination of lansoprazole in the elderly is slightly delayed.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard 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.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sugar spheres(sucrose and maize starch)
Sodium laurilsulphate
Meglumine
Mannitol
Hypromellose
Macrogol
Talc
Polysorbate 80
Titanium dioxide (E171)
Methacrylic Acid-Ethyl Acrylate Copolymer, 1:1, Dispersion 30%

Capsule shell:

Gelatin
Titanium dioxide (E171)
Quinoline yellow (E104) – only 15 mg capsules

6.2 Incompatibilities

Not applicable

6.3 Shelf life

2 years

6.4 Special precautions for storage

Do not store above 30°C.

Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

Al/Al (OPA/Al/PVC//PVC/Al/PET) blister

7, 10, 10x1, 14, 14x1, 20, 28, 28x1, 30, 30x1, 56, 56x1, 60, 98, 98x1, 100 and 100x1 capsules

Not all pack sizes may be marketed.

[to be completed nationally]

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

ratiopharm GmbH
Graf-Arco-Strasse 3
D-89079 Ulm
Germany

[to be completed nationally]

8. MARKETING AUTHORISATION NUMBER

[to be completed nationally]

9. DATE OF FIRST AUTHRORISATION/RENEWAL OF AUTHORISATION

[to be completed nationally]

10. DATE OF REVISION OF THE TEXT

[to be completed nationally]

LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

< Lansoprazol AbZ and associated names (see Annex I) 15 mg , gastro-resistant capsules, hard >
lansoprazole

[see Annex I - to be completed nationally]

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each gastro-resistant capsule contains 15 mg lansoprazole

3. LIST OF EXCIPIENTS

Also contains sucrose (sugar).

4. PHARMACEUTICAL FORM AND CONTENTS

7 Gastro-resistant hard capsules
14 Gastro-resistant hard capsules
28 Gastro-resistant hard capsules
56 Gastro-resistant hard capsules
98 Gastro-resistant hard capsules

[to be completed nationally]

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP (MM/YYYY)

9. SPECIAL STORAGE CONDITIONS

Do not store above 30°C.
Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

ratiopharm GmbH
Graf-Arco-Strasse 3
D-89079 Ulm
Germany

[to be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)

[to be completed nationally]

13. BATCH NUMBER

BN

14. GENERAL CLASSIFICATION FOR SUPPLY

[to be completed nationally]

15. INSTRUCTIONS ON USE

Acid repressive gastrointestinal-therapeutic

16. INFORMATION IN BRAILLE

< Lansoprazol AbZ 15 mg >

[to be completed nationally]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS
--

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

< Lansoprazol AbZ and associated names (see Annex I) 15 mg , gastro-resistant capsules, hard >

[see Annex I - to be completed nationally]

2. NAME OF THE MARKETING AUTHORISATION HOLDER
--

ratiopharm GmbH

[to be completed nationally]

3. EXPIRY DATE

EXP (MM/YYYY)

4. BATCH NUMBER

BN

5. OTHER

PARTICULARS TO APPEAR ON THE OUTER PACKAGING AND THE IMMEDIATE PACKAGING

OUTER CARTON

1. NAME OF THE MEDICINAL PRODUCT

< Lansoprazol AbZ and associated names (see Annex I) 30 mg , gastro-resistant capsules, hard >
lansoprazole

[see Annex I - to be completed nationally]

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each gastro-resistant capsule contains 30 mg lansoprazole

3. LIST OF EXCIPIENTS

Also contains sucrose (sugar).

4. PHARMACEUTICAL FORM AND CONTENTS

7 Gastro-resistant hard capsules
14 Gastro-resistant hard capsules
28 Gastro-resistant hard capsules
56 Gastro-resistant hard capsules
98 Gastro-resistant hard capsules

[to be completed nationally]

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP (MM/YYYY)

9. SPECIAL STORAGE CONDITIONS

Do not store above 30°C.
Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE
--

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

ratiopharm GmbH
Graf-Arco-Strasse 3
D-89079 Ulm
Germany

[to be completed nationally]

12. MARKETING AUTHORISATION NUMBER(S)
--

[to be completed nationally]

13. BATCH NUMBER

BN

14. GENERAL CLASSIFICATION FOR SUPPLY
--

[to be completed nationally]

15. INSTRUCTIONS ON USE

Acid repressive gastrointestinal-therapeutic

16. INFORMATION IN BRAILLE

< Lansoprazol AbZ 30 mg >

[to be completed nationally]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS
--

BLISTER

1. NAME OF THE MEDICINAL PRODUCT

< Lansoprazol AbZ and associated names (see Annex I) 30 mg , gastro-resistant capsules, hard >

[see Annex I - to be completed nationally]

2. NAME OF THE MARKETING AUTHORISATION HOLDER
--

ratiopharm GmbH

[to be completed nationally]

3. EXPIRY DATE

EXP (MM/YYYY)

4. BATCH NUMBER

BN

5. OTHER

PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

< **Lansoprazol AbZ and associated names (see Annex I) 15 mg, gastro-resistant capsules, hard** >
Lansoprazol

[see Annex I - to be completed nationally]

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What *Lansoprazol AbZ* is and what it is used for
2. Before you take *Lansoprazol AbZ*
3. How to take *Lansoprazol AbZ*
4. Possible side effects
5. How to store *Lansoprazol AbZ*
6. Further information

1. WHAT *Lansoprazol AbZ* IS AND WHAT IT IS USED FOR

Lansoprazol AbZ is a medicine which reduces the amount of acid made by the stomach (selective proton pump inhibitor).

Lansoprazol AbZ is given:

- to treat ulcers in the duodenum and stomach (diagnosed through gastroscopy or X-ray)
- to treat inflammation of the gullet caused by reflux of stomach acid into the gullet (reflux oesophagitis)
- as long-term treatment to prevent a recurrence of inflammation of the gullet due to reflux of stomach acid
- to remove the bacterium *Helicobacter pylori* together with suitable antibiotics in the treatment of ulcers in the stomach or duodenum (eradication therapy) and to prevent the recurrence of ulcers in patients with *Helicobacter pylori*-related ulcers in the stomach and intestines
- in the treatment of Zollinger-Ellison syndrome (ulcer formation in the stomach and duodenum, due to increased production of a hormone which secretes stomach acid, caused by a certain type of tumour).

2. BEFORE YOU TAKE *Lansoprazol AbZ*

Do not take *Lansoprazol AbZ*

- if you are allergic (hypersensitive) to *Lansoprazol* or any of the other ingredients of *Lansoprazol AbZ*.

Take special care with *Lansoprazol AbZ*

- if you have impaired liver function (see section 3. “How to take *Lansoprazol AbZ*”)

- if you use *Lansoprazol AbZ* in combination therapy with antibiotics to eradicate *Helicobacter pylori*, you should carefully read the package leaflets of these antibiotics, too
- if you take *Lansoprazol AbZ* for longer than 1 year, therapy should be regularly monitored and the doctor should carefully consider the benefit versus risk ratio
- if you experience any problems with your eyesight following long-term use (longer than 1 year), treatment with *Lansoprazol AbZ* should be promptly discontinued and you should consult an ophthalmologist.
- Before treatment with *Lansoprazol AbZ*
 - the diagnosis of ulcers of the duodenum or stomach and inflammation of the gullet due to reflux of stomach acid should be confirmed by gastroscopy or other appropriate diagnostic measures (e.g. X-ray with contrast media)
 - a stomach ulcer with *Lansoprazol AbZ*, the possibility of a malignant stomach tumour should be excluded. Intake of *Lansoprazol AbZ* may mask the symptoms of a tumour and delay diagnosis of this condition

Lansoprazole reduces the acid content of the stomach. This can lead to an increase in the number of natural bacteria present in the gastrointestinal tract. Treatment with *Lansoprazol AbZ* therefore leads to a slightly increased risk of infections in the gastrointestinal tract, such as with salmonella and *Campylobacter*.

Children

Lansoprazol AbZ is not recommended for use in children, as its safety and efficacy have not been established in this patient group.

Elderly patients

In elderly patients, a dose adjustment may be necessary due to the slower elimination of lansoprazole. A daily dose of 30 mg should not be exceeded.

Using other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

As lansoprazole is mainly broken down by certain enzymes in the liver, interactions with other medicines that are broken down by the same enzymes are possible.

The effect of *Lansoprazol AbZ* may be influenced by the following medicines or drug groups:

Fluvoxamine (a medicine for the treatment of depression), ketoconazole and itraconazole (medicines for the treatment of fungal infections), protease inhibitors (active substances used in the treatment of the AIDS virus) and macrolides (certain types of antibiotics) may markedly raise the concentration of lansoprazole in the blood and thus increase the effect of *Lansoprazol AbZ*.

The effect of the following medicines or drug groups may be influenced by *Lansoprazol AbZ* if they are used at the same time:

Ketoconazole and itraconazole (medicines for the treatment of fungal infections)

The combination of lansoprazole and ketoconazole or itraconazole should be avoided, as the reduction in stomach acid caused by intake of *Lansoprazol AbZ* may impair the absorption of the other medicines into the blood, thus leading to an underdose.

Digoxin (cardiac glycoside)

Simultaneous administration of lansoprazole and digoxin can cause a rise in plasma digoxin concentrations. For this reason, the plasma levels of patients being treated with digoxin should be monitored and a dose adjustment of digoxin made if necessary.

Tacrolimus (medicine used to prevent rejection of a transplant)

Simultaneous use of lansoprazole causes a rise in the plasma concentrations of tacrolimus. At the beginning or end of simultaneous use of Lansoprazol AbZ, plasma tacrolimus concentrations should be monitored.

Carbamazepine (medicine used in the treatment of fits)

Caution is urged if carbamazepine and lansoprazole are used simultaneously. This combination of medicines could cause a rise in carbamazepine concentrations and a decrease in lansoprazole concentrations.

Phenytoin (medicine used in the treatment of fits and irregularities of heart rhythm)

If there is simultaneous use of lansoprazole, a dose reduction of phenytoin may be necessary. At the beginning or end of lansoprazole therapy, monitoring of plasma phenytoin concentrations is recommended.

Warfarin (medicine used to prevent blood clotting)

At the beginning or end of lansoprazole therapy in patients who are already receiving warfarin therapy, caution is urged and more frequent monitoring is recommended.

Theophylline (asthma medicine)

Lansoprazole reduces the theophylline concentration. Caution is advised if the two medicines are administered in combination.

To date, no clinically relevant interactions have been demonstrated between lansoprazole and diazepam.

An interval of at least 1 hour before or after should be allowed between administration of lansoprazole and antacids and sucralfate.

Caution is urged if lansoprazole is combined with some potent medicines, as the influence of lansoprazole on other active substances has not yet been conclusively investigated.

The effect of simultaneous administration of lansoprazole and various antibiotics (particularly clarithromycin) has not been systematically investigated. Increased interactions with other medicines are likely. Monitoring of the plasma levels of other medicines administered during simultaneous treatment with lansoprazole and antibiotics is therefore recommended.

Interactions have been observed when lansoprazole was combined with certain antibiotics such as clarithromycin and amoxicillin and in a combination of all three medicines. These affect the absorption, availability to the body, the breakdown and the elimination of these medicines. The effect of clarithromycin on lansoprazole is increased if the patient is a so-called slow metaboliser.

Taking Lansoprazol AbZ with food and drink:

It is recommended that you take *Lansoprazol AbZ* before meals, as simultaneous food intake reduces the availability of lansoprazole to the body.

Pregnancy and breast-feeding

Ask your doctor or pharmacist for advice before taking any medicine.

Use of *Lansoprazol AbZ* is not recommended during pregnancy.

Limited experience to date with the use of lansoprazole in pregnant women has produced no evidence of any side effects on the unborn child or on the pregnancy itself.

You should avoid breastfeeding while taking *Lansoprazol AbZ*, as there has been insufficient experience with its use during lactation. Based on the results of animal studies, it is thought that lansoprazole crosses into the breast milk.

When making a decision as to whether breastfeeding or therapy with *Lansoprazol AbZ* should be continued or discontinued, the benefits of breastfeeding for the child and the benefits of therapy with *Lansoprazol AbZ* for the mother should be considered.

Driving and using machines

During treatment with *Lansoprazol AbZ*, side effects such as light-headedness and fatigue may occur (see section 4. "Possible side effects"). This can reduce your responsiveness when driving a vehicle or operating machinery.

Important information about some of the ingredients of *Lansoprazol AbZ*

This medicine contains sucrose. Please consult your doctor before taking *Lansoprazol AbZ* if you know that you are intolerant to certain sugars.

3. HOW TO TAKE *Lansoprazol AbZ*

Always take *Lansoprazol AbZ* exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Lansoprazol AbZ capsules are swallowed whole with sufficient liquid (e.g. a glass of water). The capsules may be opened but the minitables inside may not be chewed or crushed. *Lansoprazol AbZ* should be taken on an empty stomach (before meals).

The usual dose is

Treatment of duodenal ulcers

The recommended dose is 2 capsules once daily (equivalent to 30 mg lansoprazole) for 2 weeks. If a two-week treatment period is not sufficient for healing to occur, treatment can be continued for a further 2 weeks at the same dose.

Treatment of stomach ulcers

The recommended dose is 2 capsules once daily (equivalent to 30 mg lansoprazole) for 4 weeks. The stomach ulcer usually heals within 4 weeks. If a four-week treatment period is not sufficient for healing to occur, treatment can be continued for a further 4 weeks at the same dose.

Treatment of inflammation of the gullet due to reflux of stomach acid

The recommended dose is 2 capsules once daily (equivalent to 30 mg lansoprazole) for 4 weeks. If a four-week treatment period is not sufficient for healing to occur, treatment can be continued for a further 4 weeks at the same dose.

Prevention of a recurrence of inflammation of the gullet due to reflux of stomach acid

The recommended dose is 1 capsule once daily (equivalent to 15 mg lansoprazole). If required, the dose can be increased to 2 capsules once daily (equivalent to 30 mg lansoprazole).

Eradication of the *Helicobacter pylori* bacterium

The recommended dose is 2 capsules twice daily (equivalent to 2 times 30 mg lansoprazole) for one week in combination with one of the following three combinations:

- a) amoxicillin 1 g twice daily + clarithromycin 500 mg twice daily,
- b) clarithromycin 250 mg twice daily + metronidazole 400-500 mg twice daily,
- c) amoxicillin 1 g twice daily + metronidazole 400-500 mg twice daily.

Please read the package leaflet of the antibacterial agents for further information.

Treatment of Zollinger-Ellison syndrome

The dosage should be adjusted on an individual patient basis and continued for as long as required under specialist medical supervision.

The recommended initial dosage is 4 capsules once daily (equivalent to 60 mg lansoprazole).

Dosages up to 180 mg daily are possible.

At dosages of more than 120 mg daily, the dose should be given in 2 divided doses (every 12 hours).

Note:

For those therapeutic indications in which a daily dose exceeding 15 mg lansoprazole is specified, gastro-resistant hard capsules containing 30 mg of medically active ingredient are also available.

Dosage in patients with impaired kidney or liver function

No dose adjustment is necessary in patients with impaired kidney function. A daily dose of 30 mg lansoprazole should not, however, be exceeded.

In patients with mildly impaired liver function, a daily dose of 30 mg lansoprazole should not be exceeded.

In patients with moderately impaired liver function, a daily dose of 15 mg lansoprazole should not be exceeded.

Patients with severely impaired liver function should not take *Lansoprazol AbZ*, nor should they be given combination therapy with clarithromycin.

If you have the impression that the effect of *Lansoprazol AbZ* is too strong or too weak, please talk to your doctor.

If you take more *Lansoprazol AbZ* than you should

you should always consult a doctor.

There has been no experience with the effects of lansoprazole overdose in humans. Daily doses of 180 mg were tolerated without any marked side effects. The side effects listed in section 4 may occur in a more severe form.

If you forget to take *Lansoprazol AbZ*

Do not take a double dose to make up for a forgotten dose.

If you stop taking *Lansoprazol AbZ*

If you take too low a dose, if you take your medicine irregularly or if you stop your treatment prematurely, this may endanger the success of your treatment or may cause relapses which are more difficult to treat. Please follow your doctor's recommendations

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, *Lansoprazol AbZ* can cause side effects, although not everybody gets them.

The following frequency data are used in the evaluation of side effects:

Very common	more than 1 in 10 persons treated
Common	less than 1 in 10, but more than 1 in 100 treated patients
Uncommon	less than 1 in 100, but more than 1 in 1,000 treated patients
Rare	less than 1 in 1,000, but more than 1 in 10,000 treated patients
Very rare	less than 1 in 10,000 persons treated, including isolated reports

Gastrointestinal disorders

Common:	nausea, vomiting, diarrhoea, stomach-ache, constipation, flatulence (sometimes accompanied by abdominal pain), upper abdominal pain.
Uncommon:	dryness of the throat or mouth, loss of appetite.
Rare:	fungal infections of the gullet, inflammation of the pancreas, inflammation of the tongue.
Very rare:	inflammation of the large intestine, inflammation of the mucous membrane of the mouth, black discolouration of the tongue.

Skin and connective tissue disorders

Common:	skin rash, nettle rash, itching.
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- Rare: skin bleeding (punctiform capillary bleeding and inflamed, mainly symmetrical skin bleeding), hair loss, excessive sweating, blood vessel inflammation with skin changes (erythema multiforme).
- Very rare: maplike rash on the mucous membranes/skin (Stevens-Johnson syndrome), severe skin damage (toxic epidermal necrolysis).

Nervous system disorders

- Common: headache, dizziness
- Rare: restlessness, drowsiness, sleep disturbances, light-headedness, depression, hallucinations, confusion, dizziness, trembling, discomfort.

Disorders of the liver and gall bladder

- Uncommon: changes in liver enzyme values.
- Rare: inflammation of the liver, jaundice

Disorders of the kidneys and urinary tract

- Rare: inflammation of the kidneys (interstitial nephritis)

Blood and lymphatic system disorders

- Rare: changes in the blood count with a reduction in the blood platelet count, an increase in the number of certain white blood corpuscles (eosinophilia), a reduced production of all blood cells, anaemia or a reduction in the number of all white blood corpuscles.
- Very rare: severe reduction in certain white blood corpuscles (agranulocytosis).

Heart disorders

- Rare: palpitations, chest pain

Vascular disorders

- Rare: accumulation of water mainly in the legs (oedema)

Disorders of the skeletal muscle, connective tissue and bones

- Rare: muscle and joint pain

Eye disorders and changes in the sensation of taste

- Uncommon: disturbances in taste
- Rare: visual disturbances

Hormonal disorders

- Very rare: enlargement of the male breast gland, milky secretions from the breast gland.

General disorders

- Common: fatigue
- Rare: fever, narrowing of the airways, swelling of tissue (angioedema).
- Very rare: allergic shock, impotence, feeling unwell.

Investigations

- Very rare: increased cholesterol and blood lipid values.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE *Lansoprazol AbZ*

Do not store above 30°C.

Store in the original package in order to protect from moisture.

Keep out of the reach and sight of children.

Do not use *Lansoprazol AbZ* after the expiry date which is stated on the carton and the blister. The expiry date refers to the last day of that month.

6. FURTHER INFORMATION

What *Lansoprazol AbZ* contains

- The active substance is lansoprazol. Each gastro-resistant capsule contains 15 mg lansoprazole.
- The other ingredients are:

Capsule content:

Sugar spheres (sucrose and maize starch), Sodium laurilsulphate, Meglumine, Mannitol, Hypromellose, Macrogol, Talc, Polysorbate 80, Titanium dioxide (E171), Methacrylic Acid-Ethyl Acrylate Copolymer (1:1), Dispersion 30%

Capsule shell:

Gelatin, Titanium dioxide (E171), Quinoline yellow (E104)

What *Lansoprazol AbZ* looks like and contents of the pack

Gastro-resistant hard capsule (Gastro-resistant capsule)

Opaque yellow cap and body.

These gastro-resistant capsules are available in blister packs containing 14, 28, 56 or 98 capsules.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:

ratiopharm GmbH, Graf-Arco-Strasse 3, D-89070 Ulm, Germany

[to be completed nationally]

Manufacturer:

LICONSA, Liberación Controlada de Sustancias Activas, S.A.

Avda. Miralcampo, Nº 7, Polígono Industrial Miralcampo, 19200 Azuqueca de Henares (Guadalajara), Spain

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder:

[to be completed nationally]

This leaflet was last approved in {MM/YYYY}.

PACKAGE LEAFLET: INFORMATION FOR THE USER

< **Lansoprazol AbZ and associated names (see Annex I) 30 mg, gastro-resistant capsules, hard** >
Lansoprazol

[see Annex I - to be completed nationally]

Read all of this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. What *Lansoprazol AbZ* is and what it is used for
2. Before you take *Lansoprazol AbZ*
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1. WHAT *Lansoprazol AbZ* IS AND WHAT IT IS USED FOR

Lansoprazol AbZ is a medicine which reduces the amount of acid made by the stomach (selective proton pump inhibitor).

Lansoprazol AbZ is given:

- to treat ulcers in the duodenum and stomach (diagnosed through gastroscopy or X-ray)
- to treat inflammation of the gullet caused by reflux of stomach acid into the gullet (reflux oesophagitis)
- as long-term treatment to prevent a recurrence of inflammation of the gullet due to reflux of stomach acid
- to remove the bacterium *Helicobacter pylori* together with suitable antibiotics in the treatment of ulcers in the stomach or duodenum (eradication therapy) and to prevent the recurrence of ulcers in patients with *Helicobacter pylori*-related ulcers in the stomach and intestines
- in the treatment of Zollinger-Ellison syndrome (ulcer formation in the stomach and duodenum, due to increased production of a hormone which secretes stomach acid, caused by a certain type of tumour).

2. BEFORE YOU TAKE *Lansoprazol AbZ*

Do not take *Lansoprazol AbZ*

- if you are allergic (hypersensitive) to *Lansoprazol* or any of the other ingredients of *Lansoprazol AbZ*.

Take special care with *Lansoprazol AbZ*

- if you have impaired liver function (see section 3. “How to take *Lansoprazol AbZ*”)

- if you use *Lansoprazol AbZ* in combination therapy with antibiotics to eradicate *Helicobacter pylori*, you should carefully read the package leaflets of these antibiotics, too
- if you take *Lansoprazol AbZ* for longer than 1 year, therapy should be regularly monitored and the doctor should carefully consider the benefit versus risk ratio
- if you experience any problems with your eyesight following long-term use (longer than 1 year), treatment with *Lansoprazol AbZ* should be promptly discontinued and you should consult an ophthalmologist.
- Before treatment with *Lansoprazol AbZ*
 - the diagnosis of ulcers of the duodenum or stomach and inflammation of the gullet due to reflux of stomach acid should be confirmed by gastroscopy or other appropriate diagnostic measures (e.g. X-ray with contrast media)
 - a stomach ulcer with *Lansoprazol AbZ*, the possibility of a malignant stomach tumour should be excluded. Intake of *Lansoprazol AbZ* may mask the symptoms of a tumour and delay diagnosis of this condition

Lansoprazole reduces the acid content of the stomach. This can lead to an increase in the number of natural bacteria present in the gastrointestinal tract. Treatment with *Lansoprazol AbZ* therefore leads to a slightly increased risk of infections in the gastrointestinal tract, such as with salmonella and *Campylobacter*.

Children

Lansoprazol AbZ may not be used in children, as its safety and efficacy have not been established in this patient group.

Elderly patients

In elderly patients, a dose adjustment may be necessary due to the slower elimination of lansoprazole. A daily dose of 30 mg should not be exceeded.

Using other medicines

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

As lansoprazole is mainly broken down by certain enzymes in the liver, interactions with other medicines that are broken down by the same enzymes are possible.

The effect of *Lansoprazol AbZ* may be influenced by the following medicines or drug groups:

Fluvoxamine (a medicine for the treatment of depression), ketoconazole and itraconazole (medicines for the treatment of fungal infections), protease inhibitors (active substances used in the treatment of the AIDS virus) and macrolides (certain types of antibiotics) may markedly raise the concentration of lansoprazole in the blood and thus increase the effect of *Lansoprazol AbZ*.

The effect of the following medicines or drug groups may be influenced by *Lansoprazol AbZ* if they are used at the same time:

Ketoconazole and itraconazole (medicines for the treatment of fungal infections)

The combination of lansoprazole and ketoconazole or itraconazole should be avoided, as the reduction in stomach acid caused by intake of *Lansoprazol AbZ* may impair the absorption of the other medicines into the blood, thus leading to an underdose.

Digoxin (cardiac glycoside)

Simultaneous administration of lansoprazole and digoxin can cause a rise in plasma digoxin concentrations. For this reason, the plasma levels of patients being treated with digoxin should be monitored and a dose adjustment of digoxin made if necessary.

Tacrolimus (medicine used to prevent rejection of a transplant)

Simultaneous use of lansoprazole causes a rise in the plasma concentrations of tacrolimus. At the beginning or end of simultaneous use of Lansoprazol AbZ, plasma tacrolimus concentrations should be monitored.

Carbamazepine (medicine used in the treatment of fits)

Caution is urged if carbamazepine and lansoprazole are used simultaneously. This combination of medicines could cause a rise in carbamazepine concentrations and a decrease in lansoprazole concentrations.

Phenytoin (medicine used in the treatment of fits and irregularities of heart rhythm)

If there is simultaneous use of lansoprazole, a dose reduction of phenytoin may be necessary. At the beginning or end of lansoprazole therapy, monitoring of plasma phenytoin concentrations is recommended.

Warfarin (medicine used to prevent blood clotting)

At the beginning or end of lansoprazole therapy in patients who are already receiving warfarin therapy, caution is urged and more frequent monitoring is recommended.

Theophylline (asthma medicine)

Lansoprazole reduces the theophylline concentration. Caution is advised if the two medicines are administered in combination.

To date, no clinically relevant interactions have been demonstrated between lansoprazole and diazepam.

An interval of at least 1 hour before or after should be allowed between administration of lansoprazole and antacids and sucralfate.

Caution is urged if lansoprazole is combined with some potent medicines, as the influence of lansoprazole on other active substances has not yet been conclusively investigated.

The effect of simultaneous administration of lansoprazole and various antibiotics (particularly clarithromycin) has not been systematically investigated. Increased interactions with other medicines are likely. Monitoring of the plasma levels of other medicines administered during simultaneous treatment with lansoprazole and antibiotics is therefore recommended.

Interactions have been observed when lansoprazole was combined with certain antibiotics such as clarithromycin and amoxicillin and in a combination of all three medicines. These affect the absorption, availability to the body, the breakdown and the elimination of these medicines. The effect of clarithromycin on lansoprazole is increased if the patient is a so-called slow metaboliser.

Taking Lansoprazol AbZ with food and drink:

It is recommended that you take *Lansoprazol AbZ* before meals, as simultaneous food intake reduces the availability of lansoprazole to the body.

Pregnancy and breast-feeding

Ask your doctor or pharmacist for advice before taking any medicine.

Use of *Lansoprazol AbZ* is not recommended during pregnancy.

Limited experience to date with the use of lansoprazole in pregnant women has produced no evidence of any side effects on the unborn child or on the pregnancy itself.

You should avoid breastfeeding while taking *Lansoprazol AbZ*, as there has been insufficient experience with its use during lactation. Based on the results of animal studies, it is thought that lansoprazole crosses into the breast milk.

When making a decision as to whether breastfeeding or therapy with *Lansoprazol AbZ* should be continued or discontinued, the benefits of breastfeeding for the child and the benefits of therapy with *Lansoprazol AbZ* for the mother should be considered.

Driving and using machines

During treatment with *Lansoprazol AbZ*, side effects such as light-headedness and fatigue may occur (see section 4. "Possible side effects"). This can reduce your responsiveness when driving a vehicle or operating machinery.

Important information about some of the ingredients of *Lansoprazol AbZ*

This medicine contains sucrose. Please consult your doctor before taking *Lansoprazol AbZ* if you know that you are intolerant to certain sugars.

3. HOW TO TAKE *Lansoprazol AbZ*

Always take *Lansoprazol AbZ* exactly as your doctor has told you. You should check with your doctor or pharmacist if you are not sure.

Lansoprazol AbZ capsules are swallowed whole with sufficient liquid (e.g. a glass of water). The capsules may be opened but the minitablets inside may not be chewed or crushed. *Lansoprazol AbZ* should be taken on an empty stomach (before meals).

The usual dose is

Treatment of duodenal ulcers

The recommended dose is 1 capsule once daily (equivalent to 30 mg lansoprazole) for 2 weeks. If a two-week treatment period is not sufficient for healing to occur, treatment can be continued for a further 2 weeks at the same dose.

Treatment of stomach ulcers

The recommended dose is 1 capsule once daily (equivalent to 30 mg lansoprazole) for 4 weeks. The stomach ulcer usually heals within 4 weeks. If a four-week treatment period is not sufficient for healing to occur, treatment can be continued for a further 4 weeks at the same dose.

Treatment of inflammation of the gullet due to reflux of stomach acid

The recommended dose is 1 capsule once daily (equivalent to 30 mg lansoprazole) for 4 weeks. If a four-week treatment period is not sufficient for healing to occur, treatment can be continued for a further 4 weeks at the same dose.

Prevention of a recurrence of inflammation of the gullet due to reflux of stomach acid

The recommended dose is 15 mg lansoprazole once daily. If required, the dose can be increased to 1 capsule once daily (equivalent to 30 mg lansoprazole).

Eradication of the *Helicobacter pylori* bacterium

The recommended dose is 1 capsule twice daily (equivalent to 2 times 30 mg lansoprazole) for one week in combination with one of the following three combinations:

- a) amoxicillin 1 g twice daily + clarithromycin 500 mg twice daily,
- b) clarithromycin 250 mg twice daily + metronidazole 400-500 mg twice daily,
- c) amoxicillin 1 g twice daily + metronidazole 400-500 mg twice daily.

Please read the package leaflet of the antibacterial agents for further information.

Treatment of Zollinger-Ellison syndrome

The dosage should be adjusted on an individual patient basis and continued for as long as required under specialist medical supervision.

The recommended initial dosage is 2 capsules once daily (equivalent to 60 mg lansoprazole).

Dosages up to 180 mg daily are possible.

At dosages of more than 120 mg daily, the dose should be given in 2 divided doses (every 12 hours).

Note:

For those therapeutic indications in which a daily dose of 15 mg lansoprazole is specified, gastro-resistant hard capsules containing 15 mg of medically active ingredient are also available.

Dosage in patients with impaired kidney or liver function

No dose adjustment is necessary in patients with impaired kidney function. A daily dose of 30 mg lansoprazole should not, however, be exceeded.

In patients with mildly impaired liver function, a daily dose of 30 mg lansoprazole should not be exceeded.

In patients with moderately impaired liver function, a daily dose of 15 mg lansoprazole should not be exceeded.

Patients with severely impaired liver function should not take *Lansoprazol AbZ*, nor should they be given combination therapy with clarithromycin.

If you have the impression that the effect of *Lansoprazol AbZ* is too strong or too weak, please talk to your doctor.

If you take more *Lansoprazol AbZ* than you should

you should always consult a doctor.

There has been no experience with the effects of lansoprazole overdose in humans. Daily doses of 180 mg were tolerated without any marked side effects. The side effects listed in section 4 may occur in a more severe form.

If you forget to take *Lansoprazol AbZ*

Do not take a double dose to make up for a forgotten dose.

If you stop taking *Lansoprazol AbZ*

If you take too low a dose, if you take your medicine irregularly or if you stop your treatment prematurely, this may endanger the success of your treatment or may cause relapses which are more difficult to treat. Please follow your doctor's recommendations

If you have any further questions on the use of this product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, *Lansoprazol AbZ* can cause side effects, although not everybody gets them.

The following frequency data are used in the evaluation of side effects:

Very common	more than 1 in 10 persons treated
Common	less than 1 in 10, but more than 1 in 100 treated patients
Uncommon	less than 1 in 100, but more than 1 in 1,000 treated patients
Rare	less than 1 in 1,000, but more than 1 in 10,000 treated patients
Very rare	less than 1 in 10,000 persons treated, including isolated reports

Gastrointestinal disorders

Common:	nausea, vomiting, diarrhoea, stomach-ache, constipation, flatulence (sometimes accompanied by abdominal pain), upper abdominal pain.
Uncommon:	dryness of the throat or mouth, loss of appetite.
Rare:	fungal infections of the gullet, inflammation of the pancreas, inflammation of the tongue.
Very rare:	inflammation of the large intestine, inflammation of the mucous membrane of the mouth, black discolouration of the tongue.

Skin and connective tissue disorders

Common:	skin rash, nettle rash, itching.
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- Rare: skin bleeding (punctiform capillary bleeding and inflamed, mainly symmetrical skin bleeding), hair loss, excessive sweating, blood vessel inflammation with skin changes (erythema multiforme).
- Very rare: maplike rash on the mucous membranes/skin (Stevens-Johnson syndrome), severe skin damage (toxic epidermal necrolysis).

Nervous system disorders

- Common: headache, dizziness
- Rare: restlessness, drowsiness, sleep disturbances, light-headedness, depression, hallucinations, confusion, dizziness, trembling, discomfort.

Disorders of the liver and gall bladder

- Uncommon: changes in liver enzyme values.
- Rare: inflammation of the liver, jaundice

Disorders of the kidneys and urinary tract

- Rare: inflammation of the kidneys (interstitial nephritis)

Blood and lymphatic system disorders

- Rare: changes in the blood count with a reduction in the blood platelet count, an increase in the number of certain white blood corpuscles (eosinophilia), a reduced production of all blood cells, anaemia or a reduction in the number of all white blood corpuscles.
- Very rare: severe reduction in certain white blood corpuscles (agranulocytosis).

Heart disorders

- Rare: palpitations, chest pain

Vascular disorders

- Rare: accumulation of water mainly in the legs (oedema)

Disorders of the skeletal muscle, connective tissue and bones

- Rare: muscle and joint pain

Eye disorders and changes in the sensation of taste

- Uncommon: disturbances in taste
- Rare: visual disturbances

Hormonal disorders

- Very rare: enlargement of the male breast gland, milky secretions from the breast gland.

General disorders

- Common: fatigue
- Rare: fever, narrowing of the airways, swelling of tissue (angioedema).
- Very rare: allergic shock, impotence, feeling unwell.

Investigations

- Very rare: increased cholesterol and blood lipid values.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE *Lansoprazol AbZ*

Do not store above 30°C.

Store in the original package in order to protect from moisture.

Keep out of the reach and sight of children.

Do not use *Lansoprazol AbZ* after the expiry date which is stated on the carton and the blister. The expiry date refers to the last day of that month.

6. FURTHER INFORMATION

What *Lansoprazol AbZ* contains

- The active substance is lansoprazol. Each gastro-resistant capsule contains 30 mg lansoprazole.
- The other ingredients are:

Capsule content:

Sugar spheres (sucrose and maize starch), Sodium laurilsulphate, Meglumine, Mannitol, Hypromellose, Macrogol, Talc, Polysorbate 80, Titanium dioxide (E171), Methacrylic Acid-Ethyl Acrylate Copolymer (1:1), Dispersion 30%

Capsule shell:

Gelatin, Titanium dioxide (E171)

What *Lansoprazol AbZ* looks like and contents of the pack

Gastro-resistant hard capsule (Gastro-resistant capsule)

Hard gelatine capsules, with opaque yellow cap and body, containing pellets with enteric coating.

These gastro-resistant capsules are available in blister packs containing 14, 28, 56 or 98 capsules.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder:

ratiopharm GmbH, Graf-Arco-Strasse 3, D-89070 Ulm, Germany

[to be completed nationally]

Manufacturer:

LICONSA, Liberación Controlada de Sustancias Activas, S.A.

Avda. Miralcampo, Nº 7, Polígono Industrial Miralcampo, 19200 Azuqueca de Henares (Guadalajara), Spain

For any information about this medicinal product, please contact the local representative of the Marketing Authorisation Holder:

[to be completed nationally]

This leaflet was last approved in {MM/YYYY}.