LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 00289/0673 and 0675

LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 00289/0674 and 0676

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LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 00289/0673 and 0675

LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 00289/0674 and 0676

LAY SUMMARY

The MHRA today granted TEVA UK Limited Marketing Authorisations (licences) for the medicinal products Lansoprazole 15mg Gastro-Resistant Capsules (PL 00289/0673) and Lansoprazole 30mg Gastro-Resistant Capsules (PL 00289/0674). These are prescription only medicines (POM) for the treatment of acid-related disorders of the upper gastro-intestinal tract, with the benefit of rapid symptom relief

Lansoprazole Gastro-Resistant Capsules contain the active ingredient lansoprazole, which acts by reducing gastric acidity, a key requirement for healing of acid-related disorders such as peptic ulcers.

No new or unexpected safety concerns arose from these applications and it was therefore judged that the benefits of taking Lansoprazole 15mg and 30mg Gastro-Resistant Capsules outweigh the risks, hence Marketing Authorisations have been granted.

LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 00289/0673 and 0675

LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 00289/0674 and 0676

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy the UK granted marketing authorisations for the medicinal products Lansoprazole 15mg and 30mg Gastro-Resistant Capsules to TEVA UK Limited (PL 00289/0673-6) on 13th December 2005. The products are prescription only medicines.

The applications were submitted as abridged applications according to Article 10.1(a)(iii) of Directive 2001/83/EC, claiming essential similarity to the original products Lanzor 15 and 30mg Magensaftresistent Kapseln (Takeda, Denmark).

The products contain the active ingredient lansoprazole and are indicated for the treatment of acid-related disorders of the upper gastro-intestinal tract, with the benefit of rapid symptom relief. Lansoprazole is also effective in combination with antibiotics in the eradication of Helicobacter pylori (*H. pylori*).

Lansoprazole is a proton pump inhibitor and inhibits gastric acid by blocking the hydrogen-potassium adenosine tri-phosphate enzyme system of the gastric parietal cell.

These applications for Lansoprazole 15mg Gastro-Resistant Capsules and Lansoprazole 30mg Gastro-Resistant Capsules were submitted at the same time and both depend on the bioequivalence study comparing the applicant's 30mg product with the Zoton capsule of the same strength. Consequently, all sections of this Scientific Discussion refer to both products.

PHARMACEUTICAL ASSESSMENT

Active substance

INN: Lansoprazole

Chemical Name: 2-[[[3-methyl-4-(2, 2, 2-trifluoroethoxy)- pyridine-2-pyridinyl]methyl] sulphinyl]-1H-benzimidazole

Molecular Formula: $C_{16}H_{14}F_3N_3O_2.S$

Molecular Weight: 369.3

Appearance: White to off-white powder

Synthesis of the drug substance from the designated starting material has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specification tests are in place for all starting materials and reagents and these are supported by relevant certificates of analysis.

Appropriate proof of structure has been supplied for the active pharmaceutical ingredient.

All potential known impurities have been identified and characterised.

An appropriate specification is provided for the active substance lansoprazole.

Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

Batch analysis data are provided and comply with the proposed specification.

Appropriate stability data have been generated and no indication of instability seen. The data support a retest period of 24 months.

Other ingredients

Other ingredients consisted of titanium dioxide, magnesium carbonate light, sugar spheres, hypromellose, triethyl citrate, methacrylic acid-ethyl acrylate copolymer, and talc in a hard gelatin capsule (which consisted of red iron oxide, gelatin, brilliant blue E133 (15mg only), black iron oxide (30mg only), titanium dioxide and gelatine). All excipients used in the capsule fill are routinely tested for compliance with their respective Ph Eur monograph. Hard gelatin capsules used comply with in-house specifications. Printing ink ingredients comply with suitable food or pharmacopoeial standards.

Gelatin used in the manufacture of the capsules is the only material of animal or human origin used. Satisfactory TSE Certificates of Suitability have been provided.

Both strength capsules are packaged in aluminium/aluminium blisters and contained in cardboard boxes. Satisfactory specifications and certificates of analysis have been provided for the packaging components.

Product development and finished product
The rationale for the type of pharmaceutical form developed and formulation variables evaluated during development have been stated and are satisfactory.

The rationale and function of each excipient added is discussed. Levels of each ingredient are typical for a product of this nature and have been optimised on the basis of results from development studies.

In vitro dissolution profiles have been generated for the proposed and reference products tested in the acid phase and buffer phase. The results showed that the product complies with the qualities required for gastroresistance as well as with the dissolution test after the gastroresistance.

Satisfactory batch formulae have been provided for the manufacture of the product along with an appropriate account of the manufacturing process. The manufacturing process has been validated and has shown satisfactory results.

The finished product specifications proposed for both release and shelf life are acceptable and provide an assurance of the quality and consistency of the finished product. The analytical methods used have been suitably validated. Batch analysis data has demonstrated compliance with the proposed release specification.

Stability of the product
All results from stability studies were within specified limits. These data support a shelf-life of 24 months for the product packaged in blister packs labelled with ‘Do not store above 25°C. Store in original package.’

Bioequivalence/bioavailability
Satisfactory Certificates of Analysis have been provided for the test and reference batches.

SPC, PIL, Labels
The SPC, PIL and Labels are pharmaceutically acceptable.

CONCLUSION
It is recommended that Marketing Authorisations are granted for these applications.

The requirements for essential similarity of the proposed and reference products have been met with respect to qualitative and quantitative content of the active substance. In addition, similar dissolution profiles have been demonstrated for the proposed and reference products.

PRECLINICAL ASSESSMENT

These applications for generic products claim essential similarity to Lanzor 15 and 30mg Magensaftresistent Kapseln (Takeda, Denmark)., which have been licensed within the EEA for over 10 years.

No new preclinical data have been supplied with these applications and none are required for an application of this type.

CLINICAL ASSESSMENT

1. BACKGROUND

Lansoprazole is a member of a class of drugs called proton pump inhibitors. These drugs inhibit gastric acid by blocking the hydrogen-potassium adenosine tri-phosphatase enzyme system (the 'proton pump') of the gastric parietal cell. They are the treatment of choice for stricturing and erosive oesophagitis. The suspension formulation is especially useful to patients with difficulty in swallowing such as the elderly and those with advanced oesophageal strictures. In addition, proton pump inhibitors offer effective short-term therapy for gastric and duodenal ulcer; they are also used in combination with antibiotics for the eradication of H. pylori.

2. INDICATIONS

Uses:
Lansoprazole is effective in the treatment of acid-related disorders of the upper gastro-intestinal tract, with the benefit of rapid symptom relief. Lansoprazole is also effective in combination with antibiotics in the eradication of Helicobacter pylori (H. pylori).

Indications:
Healing and long term management of Gastro Oesophageal Reflux Disease (GORD).

Healing and maintenance therapy for patients with duodenal ulcer.

Relief of reflux-like symptoms (e.g. heartburn) and/or ulcer-like symptoms (e.g. upper epigastric pain) associated with acid-related dyspepsia.

Healing of benign gastric ulcer.

Treatment and prophylaxis of NSAID-associated benign gastric ulcers, duodenal ulcers and relief of symptoms in patients requiring continued NSAID treatment.

Long term management of pathological hypersecretory conditions including Zollinger-Ellison syndrome.

Lansoprazole is also effective in patients with benign peptic lesions, including reflux oesophagitis, unresponsive to H_2 receptor antagonists.

Eradication of H. pylori from the upper gastrointestinal tract in patients with duodenal ulcer or gastritis when used in combination with appropriate antibiotics in patients with gastritis or duodenal ulcer leading to the healing and prevention of relapse of the ulcer.

Assessor's Comment
These are consistent with those of the reference product license.

3. DOSE & DOSE SCHEDULE

These are in line with those of the reference product license.

4. TOXICOLOGY

No new data are provided or needed. However, the applicant has submitted a Preclinical Expert summary.

5. CLINICAL PHARMACOLOGY

5.1 Pharmacodynamics

Lansoprazole acts by inhibiting, specifically, the Hydrogen/Potassium ATPase (proton pump) of the parietal cell in the stomach, the terminal step in acid production. This leads to the reduction of gastric acidity, a key requirement for healing of acid-related disorders such as peptic ulceration. A single dose of 30mg inhibits pentagastrin-stimulated acid secretion by approximately 80%, indicating effective acid inhibition from the first day of dosing.

5.2 Pharmacokinetics

Peak plasma levels occur within 1.5 to 2 hours following oral administration of Lansoprazole. It has high bioavailability (80-90%). The plasma elimination half-life ranges from 1 to 2 hours after single or multiple doses in healthy subjects. Its plasma protein binding is high at 97%. Lansoprazole exhibits a prolonged pharmacological action providing effective acid suppression over 24 hours. Lansoprazole is metabolised substantially by the liver and is excreted by both the renal and biliary route.

5.3 Bioequivalence

Two bioequivalence studies were conducted to compare the bioavailability of 30mg of Lansoprazole gastro-resistant capsules - treatment A and the reference product following administration of a single 30mg capsule in the fasting and fed states. The clinical parts were carried out in compliance with Good Clinical Practice.

These were open-label, single-dose, randomized, two-period, two sequence, two-treatment, crossover studies designed to evaluate the comparative bioavailability of two formulations of Lansoprazole administered to healthy male and female subjects under fasting or fed conditions. Subjects were randomly assigned to one of the two dosing sequences. Concentrations of lansoprazole were measured from the plasma samples collected over a 12-hour interval after dosing in each period with a washout period of one week.

Statistical analysis was applied to quality assured data from all subjects that completed the study, with unbalanced groups if necessary. The GLM procedure SAS® was used. Analysis of variance (ANOVA) was applied to log-transformed AUCt, AUCinf, Cmax and to untransformed Kel and T half parameters. The significance of the sequence, period and treatment effects and the subject within sequence random effects were tested. A non-parametric analysis was performed on Tmax data. Using the same statistical model, the least square means, the differences between the treatments least square means and the corresponding standard errors of these differences were estimated for log-transformed AUCs and Cmax parameters. Based on these statistics, the

ratios of the geometric means for treatments and their 90% confidence intervals were calculated.

The results of the main pharmacokinetic parameters are summarised in tables 1-2 presented below.

Table 1 Summary of main Pharmacokinetic parameters of Lansoprazole (Single dose, fasting) N=54

Parameter	**Geometric Means**		**Ratio of**	**90%**	**Intra-**
	Arithmetic Means (CV%)		**Geometric**	**Confidence**	**Subject**
			Means (%)	**Interval (%)**	**(CV%)**
	Treatment A	**Treatment B**			
AUC0-t	2494.77	2465.36			
(ng*h/ml)	2928.81 (64)	3040.44 (67)	101.19	93.42-109.61	25
AUCinf	2534.94	2507.61			
(ng*h/ml)	3044.94 (73)	3173.20(77)	101.09	93.38-10943	25
Cmax	1044.86	992.29			
(ng/ml)	1108.65 (33)	11115.37(42)	105.30	94.11-117.82	36
Tmax[a] (h)	1.86(45)	1.75(42)	-	-	-
Kel[a] (1h)	0.5697(31)	0.5719(33)	-	-	-
Thalf[a] (h)	1.42 (55)	1.32(56)	-	-	-
[a]Presented as arithmetic mean (CV%) only.					

Table 2 Summary of main Pharmacokinetic parameters of Lansoprazole (Single dose, fed) - N=77

Parameter	**Geometric Means**		**Ratio of**	**90%**	**Intra-**
	Arithmetic Means (CV%)		**Geometric**	**Confidence**	**Subject**
			Means (%)	**Interval (%)**	**(CV%)**
	Treatment A	**Treatment B**			
AUC0-t	670.71	752.09			
(ng*h/ml)	961.60 (87)	1051.71(82)	89.18	74.80 – 106.32	73
AUCinf	719.88	779.36			
(ng*h/ml)	1053.08(92)	1121.52(92)	92.37	77.85 – 109.59	70
Cmax	191.29	210.58			
(ng/ml)	269.54(80)	282.67(74)	90.84	75.00 – 110.04	82
Tmax[a] (h)	4.60(26)	3.95(37)	-	-	-
Kel[a] (1h)	0.4944(40)	0.5241(36)	-	-	-
Thalf[a] (h)	1.71(58)	1.62(84)	-	-	-
[a]Presented as arithmetic mean (CV%) only.					

Fasting study:
The mean relative bioavailability of lansoprazole was 101.09%, with a 90% confidence interval of 93.38-109.43% for the ratio of the In-transformed $AUC_{inf\infty}$. The ratio of mean C_{max} In-transformed values was 105.30% with a 90% confidence interval of 94.11-117.82%. The mean T_{max} values were 1.86 and 1.75 hours for the test and reference products, respectively.

The essentially linear pharmacokinetics of Lansoprazole, particulary at this relatively low dose range, makes it likely that the lower-doses of Lansoprazole formulations also are bioequivalent to the corresponding marketed brand formulations although bioequivalence has not been assessed explicitly.

Fed study:
The mean relative bioavailability of lansoprazole was 92.37%, with a 90% confidence interval of 77.85-109.59% for the ratio of the In-transformed $AUC_{inf\infty}$ The ratio of mean C_{max} In-transformed values was 90.84% with a

90% confidence interval of 75.000-110.04%. The mean T_{max} values were 4.60 and 3.95 hours for the test and reference products, respectively. The differences between the test and reference products were not found to be statistically significant.

No serious adverse events were reported during each of the two studies. The majority of adverse events included complaints such as headache, dizziness, local pain at sites of injection, hot flushes, nausea, vomiting, loose stools etc.

Assessor's Comment

The results of the fasted study indicate unequivocal equivalence. The 90% confidence intervals for the AUC and C_{max} ratios fall within the conventional 80-125% bioequivalence range in the fasting study, but outside this range in the fed one. However, the fed study results comply with the wider 70-143% criterion. It is considered that this wider criterion can be applied in the case of lansoprazole particularly with its high intra-subject variability (70%-82%) implying a large range of blood drug levels, even when the same product is administered to the same subject on different ocassions.

The study under the fed conditions shows a delay in absorption for both reference and test products. The fed study shows both the brand and generic products have their bioavailability reduced although the generic product is more effected. However, this reduction is not clinically relevant and is consistent with literature data.

The applicant has not provided a biostudy at steady state. An adequate justification has been submitted, supported by relevent documentation, for the exemption of a multiple dose bioequivalence study. Unlike omeprazole, there appears to be no evidence of accumulation with lansoprazole. In addition, Lansoprazole exhibits linear pharmacokinetics over the relatively lower dose range (< 60mg) for this application.

6. EFFICACY

No new data are required. However, the applicant has submitted copies of several publications with a summary review of the literature confirming the effectiveness of Lansoprazole capsules.

7. SAFETY

No new data are needed. However, the applicant has provided several copies of publications with a safety review from the literature. No new safety issues have been detected.

8. EXPERT REPORT

A satisfactory clinical expert report has been submitted with appropriate CV.

9. SUMMARY OF PRODUCT CHARACTERISTICS

The text of the summary of product characteristics is essentially the same as that of the reference product licence.

10. PATIENT INFORMATION LEAFLET

This is satisfactory.

11. LABELLING

This is satisfactory.

12. DISCUSSION

Proton pump inhibitors, including Lansoprazole, have been available in the UK for many years. Their use is well established with recognised efficacy and acceptable safety.

With regards to the current application, sufficient clinical information has been submitted. When used as indicated, Lansoprazole has a favourable benefit-to-risk ratio. The hazard associated with Lansoprazole appears to be low and acceptable when considered in relation to its therapeutic benefits.

13. CONCLUSION

Marking authorisation may be granted on medical grounds.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of Lansoprazole 15 and 30mg Gastro-Resistant Capsules are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRECLINICAL

No new preclinical data were submitted and none are required for applications of this type.

EFFICACY

Bioequivalence has been demonstrated between the applicant's Lansoprazole 30mg Gastro-Resistant Capsules and Zoton 30mg capsules (Wyeth Ireland). Given that linear kinetics apply between the 15mg and 30mg capsules, that proportional formulae for the capsules have been used and that similar dissolution results have been shown for the two strengths, a separate bioequivalence study using the 15mg capsules is not considered necessary.

No new or unexpected safety concerns arise from these applications.

The SPC and PIL are satisfactory and consistent with that for the UK reference products.

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The bioequivalence study supports the claim that the applicant's products and the innovator products are interchangeable. Extensive clinical experience with lansoprazole is considered to have demonstrated the therapeutic value of the compound. The risk benefit is therefore considered to be positive.

LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 00289/0673 and 0675

LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 00289/0674 and 0676

STEPS TAKEN FOR ASSESMENT

1	The MHRA received the marketing authorisation application on 22nd December 2003
2	Following standard checks and communication with the applicant the MHRA considered the application valid on 22nd January 2004
7	The application was determined on 13th December 2005

LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 00289/0673 and 0675

LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 00289/0674 and 0676

STEPS TAKEN AFTER AUTHORISATION - SUMMARY

Date submitted	Application type	Scope	Outcome

1. NAME OF THE MEDICINAL PRODUCT

Lansoprazole 15 mg gastro-resistant capsules.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains the equivalent of 15 mg of lansoprazole

For excipients, see 6.1.

3. PHARMACEUTICAL FORM

Gastro-resistant capsule, hard.

A hard gelatin size 3 capsule with a light blue opaque cap and flesh opaque body, filled with granules.
Body and cap imprinting: 93
7350

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Uses:
Lansoprazole is effective in the treatment of acid-related disorders of the upper gastro-intestinal tract, with the benefit of rapid symptom relief. Lansoprazole is also effective in combination with antibiotics in the eradication of *Helicobacter pylori (H. pylori).*

Indications:
Healing and long term management of Gastro Oesophageal Reflux Disease (GORD).

Healing and maintenance therapy for patients with duodenal ulcer.

Relief of reflux-like symptoms (e.g. heartburn) and/or ulcer-like symptoms (e.g. upper epigastric pain) associated with acid-related dyspepsia.

Healing of benign gastric ulcer.

Treatment and prophylaxis of NSAID-associated benign gastric ulcers, duodenal ulcers and relief of symptoms in patients requiring continued NSAID treatment.

Long term management of pathological hypersecretory conditions including Zollinger-Ellison syndrome.

Lansoprazole is also effective in patients with benign peptic lesions, including reflux oesophagitis, unresponsive to H_2 receptor antagonists.

Eradication of *H. pylori* from the upper gastrointestinal tract in patients with duodenal ulcer or gastritis when used in combination with appropriate antibiotics in patients with gastritis or duodenal ulcer leading to the healing and prevention of relapse of the ulcer.

4.2. Posology and method of administration

Dosage
Gastro Oesophageal Reflux Disease: The recommended adult dosage is 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.

For long term management, a maintenance dose of Lansoprazole 15 mg or 30 mg once daily can be used dependent upon patient response.

Duodenal ulcer: Lansoprazole 30 mg once daily for 4 weeks.

For prevention of relapse, the recommended maintenance dose is Lansoprazole 15 mg once daily.

Acid-related dyspepsia: Intermittent courses, as required, of 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.

Benign gastric ulcer: Lansoprazole 30 mg once daily for 8 weeks.

Treatment of NSAID-associated benign gastric and duodenal ulcers and relief of symptoms: Lansoprazole 15 mg or 30 mg once daily for 4 or 8 weeks. Most patients will be healed after 4 weeks; for those patients not fully healed, a further 4 weeks treatment can be given.

For patients at particular risk or with ulcers that may be difficult to heal, the higher dose and/or the longer treatment duration should be used.

Prophylaxis of NSAID-associated benign gastric ulcers, duodenal ulcers and symptoms: Lansoprazole 15mg or 30mg once daily.

Hypersecretory conditions: The recommended starting dose should be Lansoprazole 60 mg once daily. The dosage should then be adjusted individually. Treatment should be continued for as long as clinically indicated.

For daily doses of 120 mg or more per day, the dose should be divided and administered twice daily.

Eradication of H. pylori: The following combinations have been shown to be effective when given for 7 days:

Lansoprazole 30 mg twice daily plus clarithromycin 250-500 mg twice daily and amoxycillin 1g twice daily or
Lansoprazole 30 mg twice daily plus clarithromycin 250-500 mg twice daily and metronidazole 400 mg twice daily or
Lansoprazole 30 mg twice daily plus amoxycillin 1g twice daily and metronidazole 400 mg twice daily.

The best eradication results are obtained when clarithromycin is combined with either amoxycillin or metronidazole. When used in combination with the recommended antibiotics, lansoprazole is associated with *H. pylori* eradication rates of up to 90%.

Eradication of *H. pylori* with any one of the above regimens has been shown to result in the healing of duodenal ulcers, without the need for continued anti-ulcer drug therapy. The risk of reinfection is low and relapse following successful eradication is, therefore, unlikely.

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.

The capsules should be swallowed whole. Do not crush or chew.

Elderly: Dose adjustment is not required in the elderly. The normal daily dosage should be given.

Children: There is no experience with lansoprazole in children.

Impaired Hepatic and Renal Function:
Lansoprazole is metabolised substantially by the liver. Clinical trials in patients with liver disease indicate that metabolism of lansoprazole is prolonged in patients when daily doses of 30mg are administered to patients with severe hepatic impairment. It is therefore recommended that the daily dose for patients with severe liver disease is individually adjusted

to 15mg or 30mg. These patients should be kept under regular supervision and a daily dosage of 30mg should not be exceeded.

There is no need to alter the dosage in patients with mild to moderate impairment of hepatic function or impaired renal function. The normal daily dose of 30 mg should not be exceeded.

4.3. Contraindications

The use of lansoprazole is contra-indicated in patients with a history of hypersensitivity to any of the ingredients of lansoprazole capsules.

4.4. Special warnings and precautions for use

In common with other anti-ulcer therapies, the possibility of malignancy should be excluded when gastric ulcer is suspected, as symptoms may be alleviated and diagnosis delayed. Similarly, the possibility of serious underlying disease such as malignancy should be excluded before treatment for dyspepsia commences, particularly in patients of middle age or older who have new or recently changed dyspeptic symptoms.

Before using lansoprazole with antibiotics to eradicate *H. pylori*, prescribers should refer to the full prescribing information of the respective antibiotics for guidance.

Lansoprazole should be used with caution in patients with severe hepatic dysfunction. These patients should be kept under regular supervision, and a daily dosage of 30mg should not be exceeded (see section 4.2 Posology and Method of Administration).

Decreased gastric acidity due to any means, including proton pump inhibitors, increases gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with acid-reducing drugs may lead to a slightly increased risk of gastrointestinal infections such as *Salmonella* and *Campylobacter*.

This medicinal product contains 83 mg of sucrose. When taken according to the dosage recommendations, the maximum daily dose supplies up to 664 mg of sucrose. This medicinal product is unsuitable in hereditary fructose intolerance, glucose-galactose malabsorption syndrome, or sucrase-isomaltase deficiency.

4.5. Interactions with other medicinal products and other forms of interaction

Lansoprazole is hepatically metabolised and studies indicate that it is a weak inducer of Cytochrome P450. There is the possibility of interaction with drugs which are metabolised by the liver. Caution should be exercised when oral contraceptives and preparations such as phenytoin, carbamazepine, theophylline, or warfarin are taken concomitantly with the administration of lansoprazole.

Clinically significant effects on NSAIDs or diazepam have not been demonstrated.

Antacids and sucralfate may reduce the bioavailability of lansoprazole. Therefore, they must be taken at least an hour prior to or after treatment with lansoprazole.

4.6. Pregnancy and lactation

There is insufficient experience to recommend the use of lansoprazole in pregnancy. Animal studies do not reveal any teratogenic effect. Reproduction studies indicate slightly reduced litter survival and weights in rats and rabbits given very high doses of lansoprazole. The use of lansoprazole in pregnancy should be avoided.

Animal studies indicate that lansoprazole is secreted in breast milk. There is no information on the secretion of lansoprazole into breast milk in humans. The use of lansoprazole during breast feeding should be avoided unless considered essential.

4.7. Effects on ability to drive and use machines

Lansoprazole is not known to affect ability to drive or operate machines.

4.8. Undesirable effects

Lansoprazole is well-tolerated, with adverse events generally being mild and transient.

The most commonly reported adverse events are headache, dizziness, fatigue and malaise.

Gastrointestinal effects include diarrhoea, constipation, abdominal pain, nausea, vomiting, flatulence and dry or sore mouth or throat.

As with other PPIs, very rarely, cases of colitis have been reported. In severe and/or protracted cases of diarrhoea, discontinuation of therapy should be considered. In the majority of cases symptoms resolve on discontinuation of therapy.

Alterations in liver function test values and, rarely, jaundice or hepatitis, have been reported.

Dermatological reactions include skin rashes, urticaria and pruritus. These generally resolve on discontinuation of drug therapy. Serious dermatological reactions are rare but there have been occasional reports of Stevens-Johnson Syndrome, toxic epidermal necrolysis and erythematous or bullous rashes including erythema multiforme. Cases of hair thinning and photosensitivity have also been reported.

Other hypersensitivity reactions include angioedema, wheezing, and very rarely, anaphylaxis. Cases of interstitial nephritis have been reported which have sometimes resulted in renal failure.

Haematological effects (thrombocytopenia, agranulocytosis, eosinophilia, leucopenia and pancytopenia) have occurred rarely. Bruising, purpura and petechiae have also been reported.

Other reactions include arthralgia, myalgia, depression, peripheral oedema and, rarely, paraesthesia, blurred vision, taste disturbances, vertigo, confusion and hallucinations.

Gynaecomastia and impotence have been reported rarely.

4.9. Overdose

There is no information on the effect of overdosage. However, lansoprazole has been given at doses up to 120 mg/day without significant adverse effects. Symptomatic and supportive therapy should be given as appropriate.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Proton pump inhibitors
ATC-code: A02BC03

Lansoprazole is a member of a class of substances 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. It is believed that the parent drug is biotransformed into its active form(s) in the acidic environment of the parietal cell, whereupon it reacts with the sulphydryl group of the H+ / K+ ATPase causing inhibition. This inhibition is reversible in vitro by intrinsic and extrinsic reducing agents. Lansoprazole's mode of action differs significantly from the H_2 antagonists which inhibit one of the three pathways involved in stimulation of acid production. A single dose of 30mg 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 *H. pylori. In vitro* studies have shown that lansoprazole has a direct antimicrobial effect on *H. pylori.*

5.2. Pharmacokinetic properties

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%.

Following absorption, lansoprazole is extensively metabolised and is excreted by both the renal and biliary route. A study with ^{14}C-labelled lansoprazole indicated that up to 50% of the dose was excreted in the urine. Lansoprazole is metabolised substantially by the liver.

5.3. Preclinical safety data

Gastric tumours have been observed in life-long studies in rats.

An increased incidence of spontaneous retinal atrophy has been observed in life-long studies in rats. These lesions which are common to albino laboratory rats have not been observed in monkeys or dogs or life-long studies in mice. They are considered to be rat specific. No such treatment related changes have been observed in patients treated continuously for long periods.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Gastro-resistant Granules:
Sugar spheres (sucrose, maize starch)
Hypromellose
Talc
Magnesium carbonate
Methacrylic acid ethylacrylate copolymer (1:1) dispersion 30%
Triethyl citrate
Titanium dioxide

Capsule shells:
Brilliant blue (E133)
Titanium dioxide (E171)
Red iron oxide (E172)
Gelatin

Ink:
Shellac
Black iron oxide (E172)
Soya lecithin
Antifoam DC 1510

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

2 years.

6.4. Special precautions for storage

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

6.5. Nature and contents of container

Blister packs (aluminium/aluminium) with 14, 15, 28, 30, 50, 56, 84, 98 and 100 gastro-resistant capsules.

6.6. Instruction for use and handling (, and disposal)

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Teva UK Limited
Brampton Road, Hampden Park
Eastbourne, BN22 9AG
England

8. MARKETING AUTHORISATION NUMBER

PL 00289/0673 and 0675

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

13/12/05

10. DATE OF REVISION OF THE TEXT

1. NAME OF THE MEDICINAL PRODUCT

Lansoprazole 30 mg gastro-resistant capsules.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains the equivalent of 30 mg of lansoprazole.

For excipients, see 6.1.

3. PHARMACEUTICAL FORM

Gastro-resistant capsule, hard.

A hard gelatin size 1 capsule with a light gray opaque cap and flesh opaque body, filled with granules.
Body and cap imprinting: 93
7351

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Uses
Lansoprazole is effective in the treatment of acid-related disorders of the upper gastro-intestinal tract, with the benefit of rapid symptom relief. Lansoprazole is also effective in combination with antibiotics in the eradication of *Helicobacter pylori* (*H. pylori*).

Indications
Healing and long term management of Gastro Oesophageal Reflux Disease (GORD).

Healing and maintenance therapy for patients with duodenal ulcer.

Relief of reflux-like symptoms (eg. heartburn) and/or ulcer-like symptoms (eg. upper epigastric pain) associated with acid-related dyspepsia.

Healing of benign gastric ulcer.

Treatment and prophylaxis of NSAID-associated benign gastric ulcers, duodenal ulcers and relief of symptoms in patients requiring continued NSAID treatment.

Long term management of pathological hypersecretory conditions including Zollinger-Ellison syndrome.

Lansoprazole is also effective in patients with benign peptic lesions, including reflux oesophagitis, unresponsive to H_2 receptor antagonists.

Eradication of *H. pylori* from the upper gastrointestinal tract when used in combination with appropriate antibiotics in patients with gastritis or duodenal ulcer leading to the healing and prevention of relapse of the ulcer.

4.2. Posology and method of administration

Dosage:
Gastro Oesophageal Reflux Disease: The recommended adult dosage is Lansoprazole 30mg 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.

For long term management, a maintenance dose of Lansoprazole 15mg or 30mg once daily can be used dependent upon patient response.

Duodenal ulcer: Lansoprazole 30mg once daily for 4 weeks.

For prevention of relapse, the recommended maintenance dose is Lansoprazole 15mg once daily.

Acid-related dyspepsia: Intermittent courses, as required, of 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.

Benign gastric ulcer: Lansoprazole 30mg once daily for 8 weeks.

Treatment of NSAID-associated benign gastric and duodenal ulcers and relief of symptoms: Lansoprazole 15 mg or 30 mg once daily for 4 or 8 weeks. Most patients will be healed after 4 weeks; for those patients not fully healed, a further 4 weeks treatment can be given.

For patients at particular risk or with ulcers that may be difficult to heal, the higher dose and/or the longer treatment duration should be used.

Prophylaxis of NSAID-associated benign gastric ulcers, duodenal ulcers and symptoms: Lansoprazole 15 mg or 30mg once daily according to the response.

Hypersecretory conditions: The recommended starting dose should be Lansoprazole 60mg once daily. The dosage should then be adjusted individually to patient needs and treatment should be continued for as long as clinically indicated.

For daily doses of 120mg or more per day, the dose should be divided and administered twice daily.

Eradication of H. pylori: The following combinations have been shown to be effective when given for 7 days:

Lansoprazole 30mg twice daily plus clarithromycin 250-500mg twice daily and amoxycillin 1g twice daily or
Lansoprazole 30mg twice daily plus clarithromycin 250-500mg twice daily and metronidazole 400mg twice daily or
Lansoprazole 30mg twice daily plus amoxycillin 1g twice daily and metronidazole 400mg twice daily.

The best eradication results are obtained when clarithromycin is combined with either amoxycillin or metronidazole. When used in combination with the recommended antibiotics, lansoprazole is associated with *H. pylori*-eradication rates of up to 90%.

Eradication of H. pylori with any one of the above regimens has been shown to result in the healing of duodenal ulcers, without the need for continued anti-ulcer drug therapy. The risk of reinfection is low and relapse following successful eradication is, therefore, unlikely.

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.

The capsules should be swallowed whole. Do not crush or chew.

Elderly: Dose adjustment is not required in the elderly. The normal daily dosage should be given.

Children: There is no experience with lansoprazole in children.

Impaired Hepatic and Renal Function: Lansoprazole is metabolised substantially by the liver. Clinical trials in patients with liver disease indicate that metabolism of lansoprazole is prolonged when daily doses of 30 mg are administered to patients with severe hepatic impairment. It is therefore recommended that the daily dose for patients with severe liver disease is individually adjusted to 15 mg or 30 mg. These patients should be kept under regular supervision and a daily dosage of 30 mg should not be exceeded.

There is no need to alter the dosage in patients with mild to moderate impairment of hepatic function or impaired renal function. The daily dose of 30mg should not be exceeded.

4.3. Contraindications

The use of lansoprazole is contra-indicated in patients with a history of hypersensitivity to any of the ingredients of Lansoprazole capsules.

4.4. Special warnings and precautions for use

In common with other anti-ulcer therapies, the possibility of malignancy should be excluded when gastric ulcer is suspected, as symptoms may be alleviated and diagnosis delayed. Similarly, the possibility of serious underlying disease such as malignancy should be excluded before treatment for dyspepsia commences, particularly in patients of middle age or older who have new or recently changed dyspeptic symptoms.

Before using lansoprazole with antibiotics to eradicate *H. pylori*, prescribers should refer to the full prescribing information of the respective antibiotics for guidance.

Lansoprazole should be used with caution in patients with severe hepatic dysfunction. These patients should be kept under regular supervision, and a daily dosage of 30mg should not be exceeded (see Section 4.2 Posology and Method of Administration).

Decreased gastric acidity due to any means, including proton pump inhibitors, increases gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with acid-reducing drugs may lead to a slightly increased risk of gastrointestinal infections such as *Salmonella* and *Campylobacter*.

This medicinal product contains 166 mg of sucrose. When taken according to the dosage recommendations, the maximum daily dose supplies up to 664 mg of sucrose. This medicinal product is unsuitable in hereditary fructose intolerance, glucose-galactose malabsorption syndrome, or sucrase-isomaltase deficiency.

4.5. Interactions with other medicinal products and other forms of interaction

Lansoprazole is hepatically metabolised and studies indicate that it is a weak inducer of Cytochrome P450. There is the possibility of interaction with drugs which are metabolised by the liver. Caution should be exercised when oral contraceptives and preparations such as phenytoin, carbamazepine, theophylline, or warfarin are taken concomitantly with the administration of lansoprazole.

No clinically significant effects on NSAIDs or diazepam have been found.

Antacids and sucralfate may reduce the bioavailability of lansoprazole. Therefore, they must be taken at least an hour prior to or after treatment with lansoprazole.

4.6. Pregnancy and lactation

There is insufficient experience to recommend the use of lansoprazole in pregnancy. Animal studies do not reveal any teratogenic effect. Reproduction studies indicate slightly reduced litter survival and weights in rats and rabbits given very high doses of lansoprazole. The use of lansoprazole in pregnancy should be avoided.

Animal studies indicate that lansoprazole is secreted in breast milk. There is no information on the secretion of lansoprazole into breast milk in humans. The use of lansoprazole during breast feeding should be avoided unless considered essential.

4.7. Effects on ability to drive and use machines

Lansoprazole is not known to affect ability to drive or operate machines.

4.8. Undesirable effects

Lansoprazole is well-tolerated, with adverse events generally being mild and transient.

The most commonly reported adverse events are headache, dizziness, fatigue and malaise.

Gastrointestinal effects include diarrhoea, constipation, abdominal pain, nausea, vomiting, flatulence and dry or sore mouth or throat.

Alterations in liver function test values and, rarely, jaundice or hepatitis, have been reported.

Dermatological reactions include skin rashes, urticaria and pruritus. These generally resolve on discontinuation of drug therapy. Serious dermatological reactions are rare but there have been occasional reports of Stevens-Johnson Syndrome, toxic epidermal necrolysis and erythematous or bullous rashes including erythema multiforme. Cases of hair thinning and photosensitivity have also been reported.

Other hypersensitivity reactions include angioedema, wheezing, and very rarely, anaphylaxis. Cases of interstitial nephritis have been reported which have sometimes resulted in renal failure.

Haematological effects (thrombocytopenia, eosinophilia, leucopenia and pancytopenia) have occurred rarely. Bruising, purpura and petechiae have also been reported.

Other reactions include arthralgia, myalgia, depression, peripheral oedema and, rarely, paraesthesia, blurred vision, taste disturbances, vertigo, confusion and hallucinations.

Gynaecomastia and impotence have been reported rarely.

4.9. Overdose

There is no information on the effect of overdosage. However, lansoprazole has been given at doses up to 120mg/day without significant adverse effects. Symptomatic and supportive therapy should be given as appropriate.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic group: Proton pump inhibitors
ATC-code: A02BC03

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. It is believed that the parent drug is biotransformed into its active form(s) in the acidic environment of the parietal cell, whereupon it reacts with the sulphydryl group of the H+ / K+ ATPase causing inhibition. This inhibition is reversible in vitro by intrinsic and extrinsic reducing agents. Lansoprazole's mode of action differs significantly from the H2 antagonists which inhibit one of the three pathways involved in stimulation of acid production. A single dose of 30mg 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 *H. pylori. In vitro* studies have shown that lansoprazole has a direct antimicrobial effect on *H. pylori.*

5.2. Pharmacokinetic properties

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%.

Following absorption, lansoprazole is extensively metabolised and is excreted by both the renal and biliary route. A study with ^{14}C-labelled lansoprazole indicated that up to 50% of the dose was excreted in the urine. Lansoprazole is metabolised substantially by the liver.

5.3. Preclinical safety data

Gastric tumours have been observed in life-long studies in rats.

An increased incidence of spontaneous retinal atrophy has been observed in life-long studies in rats. These lesions which are common to albino laboratory rats have not been observed in monkeys or dogs or life-long studies in mice. They are considered to be rat specific. No such treatment related changes have been observed in patients treated continuously for long periods.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

Gastro-resistant Granules:

Sugar spheres (sucrose, maize starch)
Hypromellose
Talc
Magnesium carbonate
Methacrylic acid ethylacrylate copolymer (1:1) dispersion 30%
Triethyl citrate
Titanium dioxide

Capsule shells:

Black iron oxide (E172)
Titanium dioxide (E171)
Red iron oxide (E172)
Gelatin

Ink:

Shellac
Black iron oxide (E172)
Soya lecithin
Antifoam DC 1510

6.2. Incompatibilities

Not applicable.

6.3. Shelf life

2 years.

6.4. Special precautions for storage

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

6.5. Nature and contents of container

Blister packs (aluminium/aluminium) with 7, 14, 15, 28, 30, 50, 56, 98 and 100 gastro-resistant Capsules

6.6. Instruction for use and handling (, and disposal)

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Teva UK Limited
Brampton Road, Hampden Park
Eastbourne, BN22 9AG
England

8. MARKETING AUTHORISATION NUMBER

PL 00289/0674 and 0676

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
13/12/05

10 DATE OF REVISION OF THE TEXT

PAGE 1: FRONT FACE (INSIDE OF REEL)

LANSOPRAZOLE 15 & 30 mg GASTRO-RESISTANT CAPSULES

PATIENT INFORMATION LEAFLET

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 further questions, please ask your doctor or pharmacist.
- This medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.

In this leaflet:

The name of your medicine is **Lansoprazole 15 mg or 30 mg Gastro-resistant Capsules.**

- The active ingredient is lansoprazole.
- The other ingredients are sucrose, maize starch, hypromellose, talc, magnesium carbonate, methacrylic acid ethylacrylate copolymer dispersion 30%, triethyl citrate, titanium dioxide (E171). The capsule shells contain: gelatin, titanium dioxide (E171) and red iron oxide (E172). In addition the 15 mg capsules contain brilliant blue FCF (E133) and the 30 mg capsules contain black iron oxide (E172). The printing ink contains shellac, black iron oxide (E172), soya lecithin and antifoam DC 1510.

The Marketing Authorisation holder and company responsible for manufacture: TEVA UK Limited, Eastbourne, BN22 9AG.

1. LANSOPRAZOLE; WHAT IT IS AND WHAT IT'S USED FOR

- Each gastro-resistant capsule contains 15 mg or 30 mg of lansoprazole.

Lansoprazole belongs to a group of drugs called proton pump inhibitors, which help to lower the amount of acid produced in the stomach.

- The product is available in pack sizes of 14, 15, 28, 30, 50, 56, 98, and 100 capsules.
- Your medicine is used for the treatment of acid indigestion, ulcers of the stomach or upper intestinal tract, including those associated with the bacteria *Helicobacter pylori* or non-steroidal anti-inflammatory drugs (NSAIDs), gastro oesophageal reflux disease (chronic acid heartburn caused by acid escaping from the stomach into the gullet), and Zollinger-Ellison syndrome.

2. BEFORE YOU TAKE LANSOPRAZOLE

Do not take Lansoprazole if you:

- Are sensitive to any of the ingredients in your medicine (listed above).

Take special care with Lansoprazole if you have:

- Liver or kidney problems, as your dose may need to be reduced by your doctor.

Be careful if you are taking any of the following:

- Oral contraceptives
- Phenytoin or carbamazepine (used to treat epilepsy)
- Theophylline (used to help your breathing)
- Warfarin (used to thin the blood)
- Other medicines for indigestion.

Pregnancy and Breast-feeding:

- Do not take Lansoprazole if you are pregnant
- If you are planning to become pregnant, or are breast-feeding, consult your doctor before taking Lansoprazole.

Important information about some of the ingredients of your medicine

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. HOW TO TAKE LANSOPRAZOLE

Your doctor has decided the dose which is suited to you. Always follow your doctor's instructions and those which are on the pharmacy label. If you do not understand these instructions, or you are in any doubt, ask your doctor or pharmacist.

The capsules should be swallowed with a drink of water. Do not crush or chew the capsules. The capsules should be taken before food. If you are taking any other antacid or anti-ulcer drug, you should take it one hour before or after Lansoprazole. If you take Lansoprazole once a day, take your dose first thing in the morning before breakfast. If you take Lansoprazole twice a day, take the first dose in the morning before breakfast and the second in the evening. The usual dosage instructions are given below:

Adults (including the elderly)

Acid indigestion:

The usual dose is 15 mg or 30 mg once daily for 2 to 4 weeks.

Treatment for ulcers caused by infection with the bacteria *Helicobacter pylori*:

The usual dose is 30 mg twice daily. Your doctor will also tell you to take one or two of the following antibiotics: clarithromycin, amoxicillin or metronidazole. The treatment will usually last for one week.

Treatment for ulcers in the stomach and upper part of the small intestine:

The usual dose is 30 mg once daily for 4 to 8 weeks. To prevent your symptoms returning, your doctor may tell you to continue taking a dose of 15 mg once daily.

PAGE 2: REAR FACE (OUTSIDE OF REEL)

Gastro-oesophageal reflux disease:
The usual dose is 30 mg once daily for 4 weeks. Your doctor may tell you to continue taking the same dose for a further 4 weeks. To prevent your symptoms returning your doctor may tell you to continue taking a dose of 15 mg or 30 mg once daily.
Treatment and prevention of stomach and duodenal ulcers caused by NSAIDs:
The usual dose is 15 mg or 30 mg once daily for 4 weeks. Your doctor may tell you to continue taking the same dose for a further 4 weeks. To prevent your symptoms returning, your doctor may tell you to continue taking a dose of 15 mg or 30 mg once daily.
Zollinger-Ellison Syndrome:
The usual starting dose is 60 mg once daily. Your doctor may then increase or decrease your dose. If your dose is more than 120 mg daily, you should take half the dose in the morning and half at night.

Patients with liver or kidney problems:
The maximum daily dose should not exceed 30 mg.

Children:
Lansoprazole is not recommended for children.

If you take more Lansoprazole than you should
If you (or someone else) swallow a lot of the capsules all together, or if you think a child has swallowed any of the capsules, contact your nearest hospital casualty department or your doctor immediately.
If you forget to take Lansoprazole.
If you forget to take a capsule, take one as soon as you remember, unless it is nearly time to take the next one. Never take two doses together. Take the remaining doses at the correct time.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Lansoprazole can have side effects.
A few people may develop an allergic reaction. This is an uncommon but very serious side effect. If you experience symptoms such as swelling of the lips, face and neck leading to severe difficulty in swallowing or breathing, you should tell your doctor immediately or go to the casualty department at your nearest hospital.
The most frequent side effects are:
- Headache, dizziness
- Tiredness, general feeling of being unwell
- Diarrhoea, constipation, abdominal pain, wind
- Nausea and/or vomiting
- Dry or sore mouth or throat.

The following side effects have also been reported:
- Rashes or itching (these usually disappear when treatment is stopped)
- Joint and muscle pain
- Depression
- Swelling (usually of the lower legs and feet)
- Changes in liver function test results.

Rare side effects are:
- Blurred vision, taste disturbances
- Hallucinations, confusion
- Pins-and-needles or numbness
- Hair thinning
- Sensitivity to light
- Kidney problems
- Jaundice (yellowing of the skin and white of the eyes)
- Hepatitis (inflammation of the liver)
- Bruise like rash
- Severe blistering, bleeding of the lips, eyes, mouth, nose and genital areas
- Blood disorders which may cause unusual tiredness or weakness, fever or chills, ulcers in your mouth or throat, unusual bleeding or unexplained bruising
- A sensation that your surroundings are spinning either up and down or from side to side.
- Enlargement of breasts in men and impotence.

Very rarely colitis (inflammation of the bowel leading to prolonged diarrhoea) may occur.

If you notice these or any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

5. STORING LANSOPRAZOLE

Keep Lansoprazole out of the reach and sight of children.
Do not store above 25°C. Store in the original package. Do not transfer to another container. Do not use Lansoprazole after the expiry date shown on the outer packaging. Return all unused medicines to your pharmacist for safe disposal.

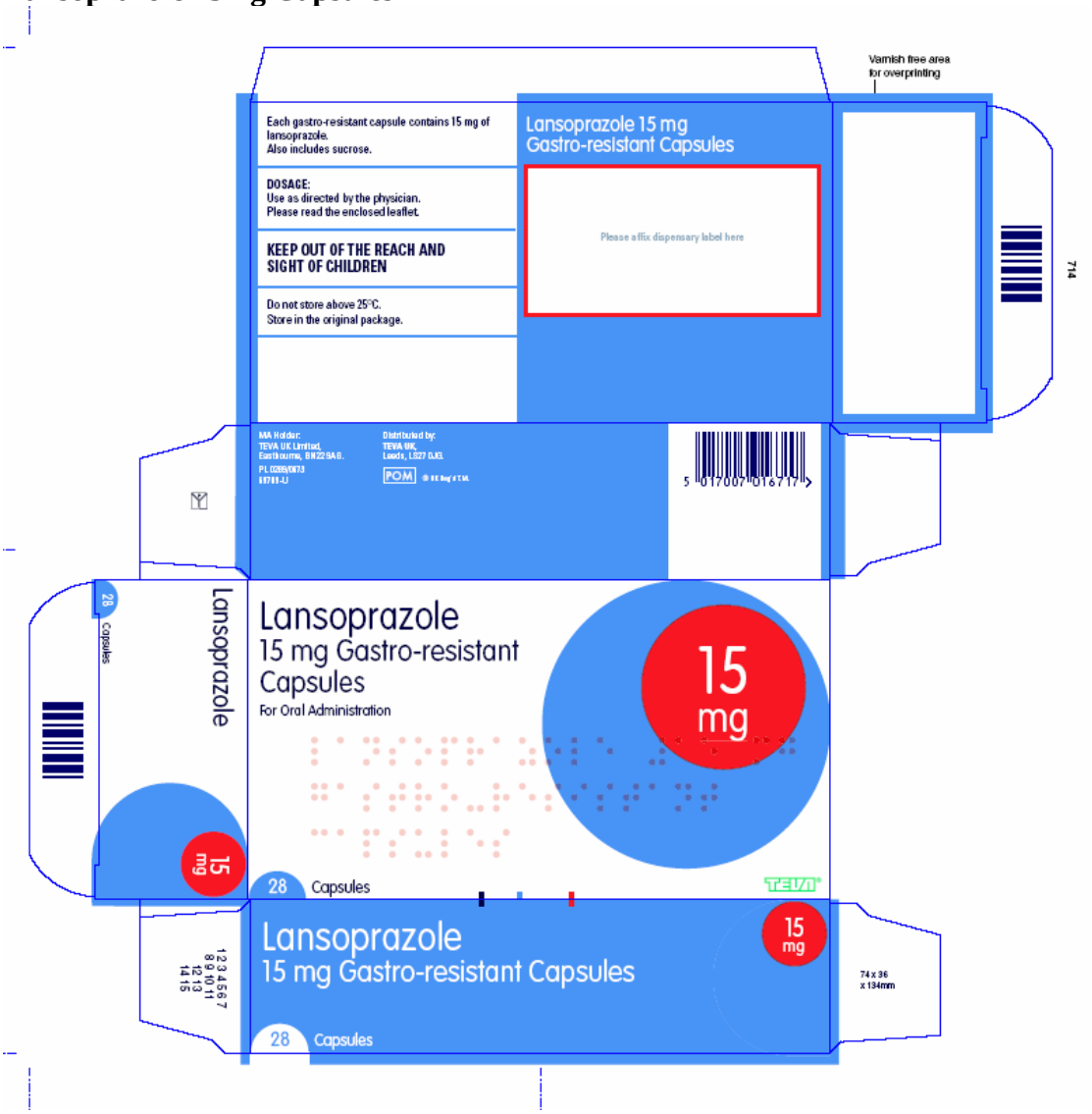
Revised: December 2005

Distributed by TEVA UK, Leeds, LS27 0JG.

TEVA UK Limited

12345-U

Lansoprazole 15mg Capsules



Lansoprazole 30mg Capsules