LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 20154/0005

LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 20154/0006

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LAY SUMMARY

The MHRA today granted Ivowen Marketing Authorisations (licences) for the medicinal products Lansoprazole 15mg Gastro-resistant Capsules (PL 20154/0005) and Lansoprazole 30mg Gastro-resistant Capsules (PL 20154/0006). 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 20154/0005

LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 20154/0006

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 Ivowen (PL 20154/0005-6) on 2nd 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 (Laboratoires Aventis, France). The UK reference products were Zoton 15mg and 30mg Capsules (Wyeth, UK).

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 Opiren 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]sulfinyl 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 shelf life of 60 months when stored protected from moisture, freezing and excessive heat (40ºC).

Other ingredients

Other ingredients consisted of sugar spheres, sodium lauril sulphate, meglumine, mannitol, hypromellose, macrogol 6000, talc, polysorbate 80, titanium dioxide, Methacrylic acid-ethyl acrylate copolymer, purified water and capsule (which consisted of quinoline yellow E104 (15mg only), titanium dioxide E171, purified water and gelatin). 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.

Satisfactory certificates of analysis have been provided for all ingredients.

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. 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 has 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.

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 gastro-resistance in acid conditions as well as satisfactory dissolution in buffer.

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 product labelled with ‘Do not store above 30°C. Store in the original package in order to protect from moisture’.

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 the original products Lanzor 15 and 30mg (Laboratoires Aventis, France), which have been licensed in the UK 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

Three bioequivalence biostudies were performed – one under fasting conditions and two under fed conditions. The fasted study involved a single dose 30mg in a crossover design in 24 subjects. Two post-prandial studies involved one with a high fat American breakfast and one with a standard fat European breakfast involving 23 and 35 subjects respectively. In each study there was a washout period of one week. These studies were carried out using the reference product. Statistical evaluations were performed using logo-transformed AUC_∞, AUC_t and C_{max} (using Wilcoxon signed rank test) and non-transformed T_{max} using Friedman's test) and non-transformed $T_{½el}$ (using ANOVA). Non-parametric test for AUC_t and C_{max} and a standard parametric test for AUC_∞ the ratio and 90% confidence intervals for all these three parameters were calculated.

The results of the main pharmaceutical parameters are summarised in tables 1-3 presented below.

Table 1 Summary of main Pharmacokinetic parameters of Lansoprazole (Single dose, fasting) N=24

	Test (Lansoprazole (A)		**Reference (B)**	
Parameters	**Mean + S.D**	**CV (%)**	**Mean + S.D**	**CV (%)**
AUC0-t (ng.h/mL)	2083.81 + 1065.44	51.13	1931.16 + 1083.46	56.10
AUC∞ (ng.h/mL)	2105.41 + 1081.51	51.37	1952.80 + 1091.68	55.90
AUCt/∞ (%)	99.01 + 0.59	0.60	98.71 + 0.81	0.82
Cmax (ng/mL)	1018.92 + 311.84	30.61	908.88 + 368.47	40.54

Tmax (h)	1.88 + 1.06	-	1.50 + 0.50	-
T½el (h)	1.08 + 0.39	36.01	1.05+ 0.36	34.56

Treatment Compararisons Lansoprazole (A) vs. Reference (B)

	AUCt	**AUC**	**Cmax**
Ratio1	103.20%	102.72%	105.43%
90% Wilcoxon's I.C.2	97.31% to 113.95%	97.28% to 113.24%	97.54% to 125.60%
Intra-subject CV	22.81%	22.57%	31.69%

1 Calculated using Hodges-Lehmann point estimator
2 Wilcoxon's (non-parametric) 90% confidence interval calculated by means of a non-parametric test (Wilcoxon's) from logo-transformed data

The test/reference ratios and the calculated 90% confidence intervals of the in transformed AUC, AUC_{0-t} and C_{max} parameters fell within the 80-125% bioequivalence range. Based on these results the test formulation Lansoprazole Capsules 30mg is bioequivalent to the reference formulation under fasting conditions.

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.

Table 2 Summary of main Pharmacokinetic parameters of Lansoprazole (Single dose, fed – High fat diet) - N=23

	Test (Lansoprazole (A)		**Reference (B)**	
Parameters	**Mean + S.D**	**CV (%)**	**Mean + S.D**	**CV (%)**
AUC0-t (ng.h/mL)	1523.21 + 1013.00	66.50	820.51 + 383.55	46.75
AUC∞ (ng.h/mL)	1708.02 + 1319.73	77.27	836.25 + 390.31	46.67
AUCt/∞ (%)	95.66 + 5.81	6.07	95.38 + 8.45	8.86
Cmax (ng/mL)	601.99 + 288.65	47.95	289.10 + 151.89	52.54
Tmax (h)	4.75 + 1.25	-	3.00 + 1.38	-
T½el (h)	1.25 + 0.65	51.98	1.12+ 0.45	39.73

Treatment Compararisons: Lansoprazole (A) vs. Reference (B)

	AUCt	**AUC***	**Cmax**
Ratio	168.37%1	211.06%2	198.17%1
90% Geometric C.I.3	-	157.30% to 283.19%	-
90% Wilcoxon's C.I.4	136.74% to 255.51.%	-	157.86% to 256.64%
Intra-subject CV	76.44%	61.37%	87.23%

* Subject No. 03 was excluded when calculating these parameters: therefore, N=22
** For T_{max}, median and IQR are calculated instead of mean and standard deviation
1 Hodges-Lehmann point estimator calculated using logo-transformed data
2 Calculated using least-squares means according to the formula $e^{(\text{lansoprazole (A) – Reference}) \times 100}$
3 90% geometric confidence interval calculated from logo-transformed data
4 90% confidence interval calculated with logo-transformed data by applying a non-parametric Wilcoxon test

Table 3 Summary of main Pharmacokinetic parameters of Lansoprazole (Single dose, fed – Standard fat diet) - N=35

	Test (Lansoprazole (A)		**Reference (B)**	
Parameters	**Mean + S.D**	**CV (%)**	**Mean + S.D**	**CV (%)**

AUC (ng.h/mL)	1602.77 + 747.00	46.61	1657.64 + 924.60	55.78
AUC (ng.h/mL)	1640.76 + 800.00	48.76	1690.25 + 390.31	56.54
AUCextra (%) p	1.788 1.833		1.922 1.803	
Cmax (ng/mL)	620.12 + 204.34	32.95	671.53 + 264.51	39.39
Tmax (h)	2.951 + 0.712	-	2.500 + 0.642	-
T½el (h)	1.29 + 0.51	39.93	1.29 + 0.45	35.20

Treatment Compararisons Lansoprazole (A) vs. Reference (B)

	Log AUCt	**Log AUC***	**Log Cmax**
Ratio	101.45%	101.29%	95.30%
90% Geometric C.I.1	92.77%-110.92%	92.73%-110.65%	86.97%-105.53
Intra-subject CV	22.06%	21.82%	25.18%

[1] 90% geometric confidence interval calculated from logo-transformed data

Comparative analyses of the relevant pharmacokinetic parameters between fed and fasting conditions for each formulation are summarised in the following table.

Pharmacokinetic Parameters	**Test (Liconsa)**		**Reference**	
	Fast	**Fed**	**Fast**	**Fed**
AUCt	2083.81 + 1065.44	1523.21 + 1013.00	1931.16 + 1083.46	820.51 + 383.55
AUC∞	2105.41 + 1081.51	1708.02 + 1319.73	1952.80 + 1091.68	836.25 + 390.31
Cmax	1018.92 + 311.84	601.99 + 288.65	908.88 + 368.47	+ 151.89

These analyses showed that food effect on AUC_t is more accentuated for the reference product than the test product. The AUC_t of the reference product decreased about 60% under fed conditions in comparison to the fasting condition results. The AUC_t arithmetic mean of the reference product decreased from 1931.16 ng.h/mL under fasting conditions to 820.51 ng.h/mL when administered with food. The test product was less affected by food as the AUC_t only decreased by 27%, going from 2083.81 ng.h/mL under fasting conditions to 1523.21 ng/h/mL when administered with food.

Food also had a significant effect on the AU_∞ of the reference product, while the effect on the same parameter was not significant for the test product. The AU_∞ arithmetic mean of the reference product went down from 1952.80 ng.h/mL in fasting conditions to 836.25 ng.h/mL when taken with food (57% decrease). For the test product, AU_∞ decreased from 2105.41 ng.h/mL in fasting conditions to 1708.02 ng.h/mL with food (19% decrease).

No serious adverse events were reported during each of the three 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 study with the standard fat breakfast shows a delay in absorption for both brand and generic products, but again show unequivocal equivalence between brand and generic. The study with the high fat meal shows the brand product has its availability reduced by 60% in line with literature data. The generic product

is not as badly affected and shows a 30% reduction in extent available. Thus the applicant's product is affected by high fat meal but not to the same extent as the brand leader. This reduction is not clinically relevant with the brand leader.

The applicant has not provided a biostudy at steady state. However, 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 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.

14. 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 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 Capsules and Opiren 30mg capsules (Almirall Prodesfarma, SA, Spain). 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 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
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LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 20154/0006

STEPS TAKEN FOR ASSESMENT

1	The MHRA received the marketing authorisation applications on 25th July 2003
2	Following standard checks and communication with the applicant the MHRA considered the applications valid on 7th October 2003
7	The applications were determined on 2nd December 2005

LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 20154/0005

LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 20154/0006

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 gastro-resistant capsule contains 15 mg of lansoprazole.

For excipients, see 6.1.

3. PHARMACEUTICAL FORM

Gastro-resistant capsule, hard.

Size 3 capsule with opaque yellow cap and body, containing white or off-white spherical microgranules.

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: 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: The recommended adult dosage is 15 mg or 30 mg once daily for 4 or 8 weeks. For patients not healed after 4 weeks, a further 4 weeks treatment can be given.

Higher doses and/or longer treatment duration should be used for patients at particular risk or with ulcers that may be difficult to heal.

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%.

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.

No dosage adjustment is necessary in patients with mild to moderate impairment of hepatic function or impaired renal function. The normal daily dose of 30mg sould 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 medicine contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

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, dyspepsia, 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 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 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 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 and maize starch)
Sodium laurilsulphate
Meglumine
Mannitol (E421)
Hypromellose
Macrogol 6000
Talc
Polysorbate 80
Titanium dioxide (E171)
Eudragit® L30-D55 (methacrylic acid-ethyl acrylate copolymer, 1:1, dispersion 30%)

Capsule Shells:

Gelatin
Titanium dioxide (E171)
Quinoline yellow (E104)
Purified water

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

Aluminium/aluminium blister.

7, 14, 15, 28, 30, 35, 56, 60 and 98 capsules.

28 and 98 capsule calendar pack.

Not all pack sizes may be marketed.

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

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Ivowen Limited
4 Emmet Place
Market Street
Clonmel
Co. Tipperary
IRELAND

8. MARKETING AUTHORISATION NUMBER

PL 20154/0005

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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 gastro-resistant capsule contains 30 mg of lansoprazole.

For excipients, see 6.1.

3. PHARMACEUTICAL FORM
Gastro-resistant capsule, hard.

Size 1 capsule with opaque white cap and body, containing white or off-white spherical microgranules.

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: Lansoprazole 15mg or 30mg 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: The recommended adult dosage is 15mg or 30mg once daily for 4 or 8 weeks. For patients not healed after 4 weeks, a further 4 weeks treatment can be given.

Higher doses and/or longer treatment duration should be used for patients at particular risk or with ulcers that may be difficult to heal.

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 in patients when daily doses of 30mg are administered to patients with severe hepatic impairment. For patients with severe hepatic impairment, it is recommended that the daily dose 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.

No dosage adjustment is necessary in patients with mild to moderate impairment of hepatic function or impaired renal function. The normal 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 medicine contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

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.

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 and maize starch)
Sodium laurilsulphate
Meglumine
Mannitol (E421)
Hypromellose
Macrogol 6000
Talc
Polysorbate 80
Titanium dioxide (E171)
Eudragit® L30-D55 (methacrylic acid-ethyl acrylate copolymer, 1:1, dispersion 30%)

Capsule Shells:

Gelatin
Titanium dioxide (E171)
Purified water

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

Aluminium/aluminium blister.

7, 14, 15, 28, 30, 35, 56, 60 and 98 capsules.

28 and 98 capsule calendar pack.

Not all pack sizes may be marketed.

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

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Ivowen Limited
4 Emmet Place
Market Street
Clonmel
Co. Tipperary

Ireland

8. MARKETING AUTHORISATION NUMBER
PL 20154/0006

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10 DATE OF REVISION OF THE TEXT

LANSOPRAZOLE 15 mg GASTRO-RESISTANT CAPSULES
LANSOPRAZOLE 30 mg GASTRO-RESISTANT CAPSULES

Read all of this leaflet carefully before you start taking this medicine. • Keep this leaflet. You may want to read it again • If you have further questions, please ask your doctor or pharmacist • This medicine has been prescribed for you personally. Do not give it to anyone else. It may harm them, even if their symptoms are the same as yours.

YOUR MEDICINE

There are two strengths of Lansoprazole Gastro-Resistant Capsules available. Each capsule contains either 15 mg or 30 mg of the active ingredient lansoprazole. It also contains maize starch, sucrose, sodium laurilsulphate, meglumine, mannitol (E421), hypromellose, macrogol, talc, polysorbate, titanium dioxide (E171) and methacrylic acid-ethyl acrylate co-polymer. The capsule shell contains gelatin, titanium dioxide (E171), and water. The 15 mg capsules also contain quinoline yellow (E104). The 15 mg capsules are yellow and the 30 mg capsules are white. Lansoprazole Gastro-Resistant Capsules are available in blister packs of 28 capsules. Your pharmacist will dispense the number of capsules prescribed by your doctor.

Product Licence Holder: Ivowen Ltd, 4 Emmet Place, Market Street, Clonmel, Co. Tipperary, Ireland.
Manufacturer and Distributor: Generics [UK] Ltd, Station Close, Potters Bar, Hertfordshire, EN6 1TL, UK.

WHAT LANSOPRAZOLE IS AND WHAT IT IS USED FOR

Your medicine is in the form of a hard 'gastro-resistant' capsule. This allows the drug to reach the stomach before being released slowly. Each capsule contains Lansoprazole which belongs to a group of medicines known as proton pump inhibitors. Lansoprazole reduces the amount of acid produced in your stomach. Lansoprazole Capsules can be used for the following conditions:

- to help treat non-cancerous gastric (stomach) ulcers and duodenal ulcers: the ulcers may be associated with NSAID (non-steroidal anti-inflammatory drug) treatment eg. Ibuprofen, or related to an infection from the bacteria *Helicobacter pylori*
- to help prevent gastric and duodenal ulcers from NSAID treatment
- to help treat and prevent ulcers caused by acid reflux (burning pain caused by stomach acid escaping back up the foodpipe)
- to help treat patients with a high gastric acid secretion (Zollinger-Ellison Syndrome)
- to help treat patients with GORD (gastro oesophageal reflux disease).

BEFORE TAKING LANSOPRAZOLE GASTRO-RESISTANT CAPSULES

Do not take this medicine and tell your doctor if you have taken Lansoprazole or any of the capsule's ingredients before, and suffered an allergic or unusual reaction. This medicine contains sucrose (sugar). If you have been told by your doctor that you have an intolerance to some sugars, consult your doctor before taking Lansoprazole Gastro-Resistant Capsules.

Tell your doctor or pharmacist if:

- you are pregnant or plan to become pregnant
- you are breast feeding
- you have severe liver problems
- you are taking any of the following medicines: * oral contraceptives * antiepileptics eg. Phenytoin, Carbamazepine * Theophylline, for asthma * Warfarin, to thin the blood * antacids, to relieve indigestion or Sucralfate, for ulcers: take at least one hour before or after Lansoprazole treatment.

HOW TO TAKE LANSOPRAZOLE GASTRO-RESISTANT CAPSULES

- Swallow the capsules whole with a full glass of water before food
- Do not chew or crush the capsules
- Take this medicine as directed by your doctor.

The doses below are used to treat the following conditions.

ADULTS (including the elderly)

To treat duodenal or stomach ulcers - Take one 30 mg capsule of Lansoprazole once daily. Treatment for duodenal ulcers is usually for 4 weeks and for gastric ulcers, 8 weeks. For ulcers related to non-steroidal anti-inflammatory drug (NSAID) treatment, the usual dose is 15 mg or 30 mg once a day for 4 or 8 weeks. To prevent recurrence of these ulcers and symptoms, the usual dose is 15 mg or 30 mg of Lansoprazole once a day.

To treat ulcers related to *H. pylori* infection - Take 30 mg of Lansoprazole twice daily for 1 week. Your doctor will also prescribe two antibiotics to be taken along with your Lansoprazole Capsules. Your doctor will tell you how and when to take your medicines. Follow your doctor's instructions carefully.

Zollinger-Ellison Syndrome - Take 60 mg of Lansoprazole once a day. Your doctor may need to increase this dose. For doses of 120 mg or more a day, take the medicine in two doses, one in the morning and one in the evening. Your doctor will tell you how and when to take your medicine.

To treat acid reflux (reflux oesophagitis, gastroesophageal reflux disease) - To treat the symptoms of acid reflux, take 15 mg or 30 mg once daily for 2-4 weeks. If symptoms do not improve, go back to your doctor. *To treat GORD,* take 30 mg of Lansoprazole once daily for 4 weeks. In some cases patients may need to continue treatment for another 4 weeks. *To prevent relapse of the symptoms of GORD,* the usual dose is 15 mg or 30 mg of Lansoprazole a day. Patients with severe liver problems should not take more than 30 mg Lansoprazole a day.

CHILDREN - Do not give Lansoprazole Gastro-Resistant Capsules to children.

If you forget to take a dose, take it as soon as you remember. However, if it is almost time for your next dose, do not take the missed dose, take the next dose on time. Never take a double dose or two doses one after the other.

If you take too much of your medicine, tell your doctor immediately or go to your nearest casualty department.

POSSIBLE SIDE EFFECTS

Like most medicines, Lansoprazole can have side effects. The most common effects are headache, dizziness, feeling tired or generally unwell, diarrhoea or constipation, feeling or being sick, stomach pain, indigestion, wind, and a dry or sore mouth or throat. Some patients may suffer from skin rashes or itchy red skin. These effects go away when treatment is stopped.

Stop taking Lansoprazole and tell your doctor immediately or go to your nearest casualty department if you suffer from: • swelling of the lips, tongue or face or have difficulty breathing • a severe skin rash (red, tender, itchy, burning, or peeling skin) • and feel feverish.
These are rare allergic reactions.

Some patients may suffer from hair loss, skin sensitive to light or kidney problems. **Tell your doctor** if you notice unusual bruising or bleeding of the skin, other skin reactions, liver problems and yellowing of the skin or whites of the eyes. These effects are rare but you may need medical attention.

Other side effects include joint or muscle pain, depression, swelling of the lower legs or hands and rarely, numbness or tingling in the hands and feet, blurred vision, taste changes, vertigo, confusion, hallucinations, breast changes and impotence.

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

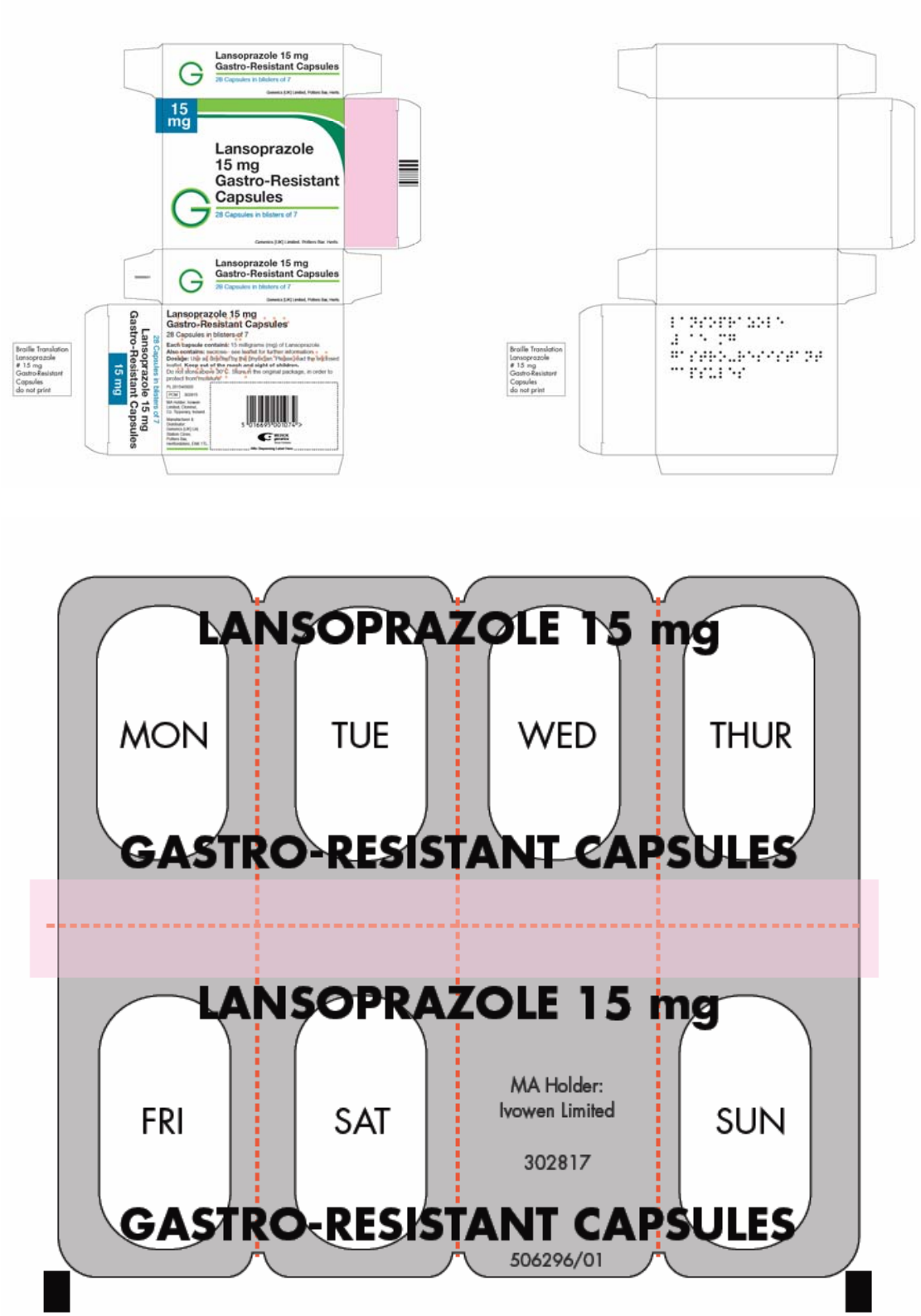
STORING LANSOPRAZOLE GASTRO-RESISTANT CAPSULES

- Keep this medicine out of the reach and sight of children
- Do not store above 30°C
- Store in the original package in order to protect from moisture.

Do not take this medicine after the expiry date shown on the label.
On the label you will find the letters 'Exp' followed by some numbers. These numbers are the date when the medicine is no longer fit for use. Do not use this medicine after this date.

Date of leaflet preparation: March 2005 303110 50905/01

Lansoprazole 15mg Capsules



Lansoprazole 30mg Capsules