LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES (LANSOPRAZOLE) PL 04147/0052

LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES (LANSOPRAZOLE) PL 04147/0053

UK Public Assessment Report

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LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES (LANSOPRAZOLE) PL 04147/0053

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Medo Pharmaceuticals Limited Marketing Authorisations (licences) for the medicinal products Lansoprazole 15mg Gastro-Resistant Capsules (PL 04147/0052) and Lansoprazole 30mg Gastro-Resistant Capsules (PL 04147/0053) on 20th April 2007. These are prescription-only medicines (POM) used 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 belongs to a group of medicines called proton pump inhibitors and acts by reducing the amount of acid the stomach makes.

The test products were considered the same as the reference products Zoton Capsules 15mg and Zoton Capsules 30mg (PL 00011/0288 & 00011/0288, John Wyeth and Brother Limited) based on the data submitted by Medo Pharmaceuticals Limited.

These applications are based on reference products with valid UK licences. No new or unexpected safety concerns arose from these applications and it was therefore judged that the benefits of taking Lansoprazole 15mg Gastro-Resistant Capsules and Lansoprazole 30mg Gastro-Resistant Capsules outweigh the risks; hence Marketing Authorisations (MAs) have been granted.

LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES (LANSOPRAZOLE) PL 04147/0052

LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES (LANSOPRAZOLE) PL 04147/0053

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted Medo Pharmaceuticals Limited Marketing Authorisations for the medicinal products Lansoprazole 15mg Gastro-Resistant Capsules (PL 04147/0052) and Lansoprazole 30mg Gastro-Resistant Capsules (PL 04147/0053) on 20th April 2007. The products are prescription-only medicines.

These are abridged applications, one complex and one standard, for Lansoprazole 15mg Gastro-Resistant Capsules and Lansoprazole 30mg Gastro-Resistant Capsules respectively. These are two strengths of lansoprazole, submitted under Article 10.1 of Directive 2001/83/EC, as amended, claiming to be generic medicinal products of the reference products Zoton Capsules 15mg and Zoton Capsules 30mg respectively (PL 00011/0288 & 00011/0287, granted to John Wyeth and Brother Limited on 26/01/2004). PL 00011/0288 was a Change of Ownership (CoA) from PL 00095/0302, granted to Cyanamid of GB Ltd. on 17/01/1996, which was an abridged complex application referencing PL 00095/0264 granted to Cyanamid of GB Ltd. on 23/02/1994. This was the innovator product. The reference products have been authorised in the UK since February 1994 (30mg strength) and January 1996 (15mg strength) and so the 10-year period of data exclusivity has expired.

The products contain the active ingredient lansoprazole, a member of the class of drugs called proton pump inhibitors, which reduce gastric acidity, an important factor in healing acid-related disorders such as gastric ulcer, duodenal ulcer and reflux oesophagitis. It is used to treat gastro-oesophageal reflux disease, ulcers, acid-related dyspepsia and hypersecretory conditions (Zollinger-Ellison syndrome).

Lansoprazole is also effective in combination with antibiotics in the eradication of Helicobacter pylori (H. pylori), although for these particular generic products, advice related to the treatment of H pylori is not included in the product literature. These parts of the licence are, therefore, dissimilar to those of the reference product.

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 two bioequivalence studies presented comparing the applicant's 30mg product with the reference product Agopton 30mg DR Capsules, Takeda Pharma GmbH (Zoton Capsules 30mg is the UK marketed version of the German product Agopton 30mg DR Capsules). Consequently, all sections of the Scientific Discussion refer to both products. As the test products, Lansoprazole 15mg Gastro-Resistant Capsules and Lansoprazole 30mg Gastro-Resistant Capsules, were deemed to meet the criteria specified in the Note for Guidance on the investigation of bioavailability and bioequivalence (CPMP/EWP/QWP/1401/98), the results and conclusions of the bioequivalence studies on the 30mg strength were extrapolated to the 15mg strength tablets.

PHARMACEUTICAL ASSESSMENT

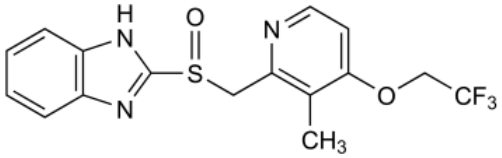
ACTIVE SUBSTANCE

Lansoprazole

Nomenclature:

INN:	Lansoprazole
Chemical name:	2-[[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]sulfiny1]1H-benzimidazole

Structure:



Molecular formula:	$C_{16}H_{14}F_3N_3O_2S$
Molecular weight:	369.3
CAS No:	103577-45-3
Physical form:	White to off white powder
Solubility:	Lansoprazole is very slightly soluble in water, soluble in methanol, sparingly soluble in ethanol, freely soluble in N, N-dimethylformamide. It dissolves in dilute solutions of sodium hydroxide.
Chirality:	Lansoprazole has a chiral centre, but is manufactured as a racemic mixture.

Lansoprazole is not described in the British Pharmacopeia (BP) or European Pharmacopeia (EP), but a US Pharmacopeia (USP) monograph is available.

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 specifications are in place for all starting materials and reagents and these are supported by relevant Certificates of Analysis. Confirmation has been provided that the raw materials, intermediates and auxiliary agents used in synthesis of the active are not of animal, biological or genetically modified origin, and therefore comply with the TSE requirements.

An appropriate active substance specification has been provided which was set by the DMF (Drug Master File) holder and is in line with the US Pharmacopeia monograph specification. 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.

Satisfactory Certificates of Analysis have been provided for reference standards used by the active substance manufacturer during validation studies.

Active lansoprazole is stored in appropriate packaging. It is packaged in colourless LDPE (low density polyethylene) bags placed in black LDPE bags, both sealed with plastic closings, with silica gel between bags. The sealed bags are packed into drums. Specifications and Certificates of Analysis have been provided for the packaging materials used. The LDPE bags in direct contact with the drug substance satisfy Directive 2002/72/EC (as amended), and are suitable for contact with foodstuffs.

Appropriate stability data have been generated for active substance stored in the proposed commercial packaging. This data demonstrates the stability of the drug substance and supports a retest period of 5 years when stored protected from moisture, freezing and excessive heat (40°C), and in the proposed packaging.

DRUG PRODUCT

Description and Composition

The drug products are presented as hard gelatin capsules containing white or almost white, gastro-resistant tablets. The capsules contain 15mg or 30mg of the active ingredient lansoprazole.

Other ingredients consist of pharmaceutical excipients, namely lactose monohydrate, hypromellose, purified water, crospovidone, and glyceryl dibehenate making up the gastro-resistant tablets; and titanium dioxide (E171), silicon dioxide, hypromellose, micronised talc, triethyl citrate, methacrylic acid copolymer, and purified water making up the tablet coating. The excipients making up the capsule with its markings are gelatin, titanium dioxide, black printing ink, and water. Appropriate justification for the inclusion of each excipient has been provided.

All excipients used comply with their respective European Pharmacopoeia monographs, with the exception of glyceryl dibehenate which complies with the USP, and the black printing ink which complies with the European Directive. Satisfactory Certificates of Analysis have been provided for all excipients.

The only excipients used that contain material of animal or human origin are gelatin and lactose monohydrate. Certificates of Suitability have been provided by all the gelatin suppliers stating that the gelatin they provide meets the criteria described in the current version of the monograph ‘Products with risk of transmitting agents of animal spongiform encephalopathies’.

The applicant has provided a declaration that milk used in the production of lactose monohydrate is sourced from healthy animals under the same conditions as that for human consumption.

There were no novel excipients used.

In the manufacturing process, a 5% overage of the active ingredient solution is used. Overages at the different stages have also been declared for some of the excipients. All of the overages are used to compensate for manufacturing losses.

Dissolution and impurity profiles

Dissolution profiles for the drug products were found to be similar to those for the reference products.

Impurity profiles for the drug products were found to be similar to those for the reference products, and all the impurities are within the specification limits.

Pharmaceutical development

Details of the pharmaceutical development of the drug products have been supplied and are satisfactory.

Manufacture

A description and flow-chart of the manufacturing method has been provided.

In-process controls are appropriate considering the nature of the product and the method of manufacture. Process validation studies have been conducted and are satisfactory.

Finished product specification

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 products. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. Test methods have been described and have been adequately validated, as appropriate. Batch data have been provided and comply with the release specification. Certificates of Analysis have been provided for any reference standards used.

Container Closure System

Two types of container closure systems are proposed:

(1) Aluminium/aluminium blister - pack sizes 28 and 56. The 30mg strength capsules are additionally licensed in pack sizes of 7, 14, and 42

(2) HDPE (high density polyethylene) bottle with polypropylene cap - pack size 50

The blister strips / HDPE bottles are packaged with the PIL (Patient Information Leaflet) into cardboard outer cartons The MAH (Marketing Authorisation Holder) has stated that not all pack sizes will be marketed.

Specifications and Certificates of Analysis for all packaging components used have been provided. These are satisfactory.

All primary product packaging complies with EU legislation, Directive 2002/72/EC (as amended), and is suitable for contact with foodstuffs.

Stability

Finished product stability studies have been conducted in accordance with current guidelines and results were within the proposed specification limits. Based on the results, a shelf-life of 18 months has been set for Lansoprazole 15mg Gastro-Resistant

Capsules supplied in blisters or bottles, as well as for Lansoprazole 30mg Gastro-Resistant Capsules supplied in blisters; and a shelf-life of 24 months has been set for Lansoprazole 30mg Gastro-Resistant Capsules supplied in bottles. The shelf-lives are satisfactory. Storage conditions are 'Do not store above 25°C' and 'Store in the original container'.

Bioequivalence Study

Two bioequivalence studies were presented comparing the test product, Lansoprazole 30mg Gastro-Resistant Capsules, to the reference product, Agopton 30mg DR Capsules (Takeda Pharma GmbH).

An evaluation of the bioequivalence studies is found in the Clinical Assessment section.

Product Information

The approved SmPCs, leaflets, and labelling are satisfactory.

Conclusion

The test products are pharmaceutically equivalent to the reference products which have been licensed in the UK for over 10 years. The drug products correspond to the current EU definition of a generic medicinal product because they comply with the criteria of having the same qualitative and quantitative composition in terms of the active substance and pharmaceutical form. On this basis, and considering the bioequivalence data provided, the applicant's claim that Lansoprazole 30mg Gastro-Resistant Capsules is a generic medicinal product of Zoton Capsules 30mg appears justified. As the test products, Lansoprazole 15mg Gastro-Resistant Capsules and Lansoprazole 30mg Gastro-Resistant Capsules, meet all the criteria as specified in the Note for Guidance on the investigation of bioavailability and bioequivalence (CPMP/EWP/QWP/1401/98), the results and conclusions of the bioequivalence studies on the 30mg strength were extrapolated to the 15mg strength tablets.

All pharmaceutical issues have been resolved and the quality grounds for these applications are considered adequate. It is recommended that Marketing Authorisations are granted.

PRECLINICAL ASSESSMENT

These abridged applications, submitted under Article 10.1 of Directive 2001/83/EC, as amended, are for Lansoprazole 15mg Gastro-Resistant Capsules and Lansoprazole 30mg Gastro-Resistant Capsules, products claiming to be generic medicinal products of Zoton Capsules 15mg and Zoton Capsules 30mg (John Wyeth and Brother Limited) respectively, 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 applications of this type.

CLINICAL ASSESSMENT

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.

INDICATIONS

Lansoprazole 15mg Gastro-Resistant Capsules and Lansoprazole 30mg Gastro-Resistant Capsules are indicated for the treatment of acid-related disorders of the upper gastro-intestinal tract, such as gastric ulcer, duodenal ulcer and reflux oesophagitis. They are used to treat gastro-oesophageal reflux disease, ulcers, acid-related dyspepsia and hypersecretory conditions (Zollinger-Ellison syndrome).

The indications are consistent with those for the innovator product and are satisfactory.

POSOLOGY AND METHOD OF ADMINISTRATION

The posology is consistent with that for the innovator product and is satisfactory.

TOXICOLOGY

No new data has been submitted and none are required for this type of application.

CLINICAL PHARMACOLOGY

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.

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.

Pharmacokinetics - Bioequivalence studies

The applicant presented two bioequivalence studies comparing the test product, Lansoprazole 30mg Gastro-Resistant Capsules, to the reference product, Agopton 30mg DR Capsules (Takeda Pharma GmbH), marketed in Germany.

Two bioequivalence studies were performed – one under fasting conditions and one under fed conditions. Both the studies involved a single dose 30mg lansoprazole in a crossover 4-period, 2-sequence design and conducted in healthy male and female subjects. A total of 52 were recruited into the studies with 42 completing and having their data analysed. In each study there was a washout period of one week. Drug concentration measurements were performed using a validated HPLC/UV assay. LLOQ (lower limit of quantification) was 5.01ng/ml and the linearity was proven up to 2000ng/ml.

Statistical and pharmacokinetic analyses were generated. The untransformed and in-transformed pharmacokinetic parameters were statistically analysed using a random ANOVA model adjusting for the study groups. Standard statistical tests for AUC_{∞}, AUC_t and C_{max} and 90% confidence intervals (CI) were performed for all these in-transformed parameters.

The results of the main pharmaceutical parameters are summarised in Tables 1 & 2 presented below.

Table 1 - Summary of main Pharmacokinetic parameters of Lansoprazole (Single 30mg dose, fasting) N=42

Parameter	**Geometric LS Mean Arithmetic Mean (CV%)**	
	TEST-FAST	**REFERENCE-FAST**
C_{max} (ng/ml)	769.73 792.0 (41.7)	963.41 1010.7 (35.8)
AUC_T (ng-h/mL)	1876.11 2191.5 (75.7)	1957.37 2297.6 (73.3)
AUC_{∞} (ng-h/mL)	1936.96 2303.9 (85.2)	2012.76 2408.3 (83.7)
T_{max}* (h)	2.33 (33.9)	1.33 (41.3)
$T_{1/2el}$(h)	1.31 (51.5)	1.31 (58.6)

* the median is presented.

STATISTICAL EVALUATION: TEST *versus* REFERENCE

	GEOMETRIC LS MEANS			**90% CONFIDENCE LIMITS**	
PARAMETER	**TEST**	**REFERENCE**	**RATIO**	**LOWER**	**UPPER**
C_{max}	769.73	963.41	79.90	72.84	87.63
AUC_T	1876.11	1957.37	95.85	91.21	100.72
AUC_{∞}	1936.96	2012.76	96.23	91.49	101.23

Table 2 - Summary of main Pharmacokinetic parameters of Lansoprazole (Single 30mgdose, fed) - N=42

Parameter	Geometric LS Mean Arithmetic Mean (CV%)	
	TEST-FED	**REFERENCE-FED**
C_{max} (ng/ml)	650.79 725.7 (53.6)	252.06 305.8 (68.9)
AUC_T (ng-h/mL)	1838.90 2173.9 (67.0)	736.27 999.3 (97.7)
AUC_∞ (ng-h/mL)	1988.98 2505.6 (77.1)	817.74 1131.3 (102.7)
T_{max}* (h)	6.00 (28.0)	3.50 (23.6)
$T_{1/2el}$(h)	1.49 (56.9)	1.31 (65.5)

* the median is presented.

STATISTICAL EVALUATION: TEST *versus* REFERENCE

	GEOMETRIC LS MEANS			**90% CONFIDENCE LIMITS**	
PARAMETER	**TEST**	**REFERENCE**	**RATIO**	**LOWER**	**UPPER**
C_{max}	650.79	252.06	258.19	211.62	315.01
AUC_T	1838.90	736.27	249.76	211.04	295.58
AUC_∞	1988.98	817.74	243.23	207.70	284.84

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

Discussion of bioequivalence studies

The results of the fasting study demonstrate bioequivalence. The 90% confidence intervals (CI) for the AUC and C_{max} ratios fall within the conventionally acceptable range of 80-125% and 70-143% respectively. The 90% CI in the fed study were outside these ranges.

The data, outside the conventional bioequivalence range of CI, displayed in the fed study can be accepted in the case of lansoprazole particularly with its high intra-

subject variability. This implies a large range of blood drug levels, even when the same product is administered to the same subject on different occasions.

The fasting study shows a delay in absorption for test product compared with the reference product. The fed study shows that both the test and reference products have their rates of absorption prolonged although the test product is more affected. However, this prolongation is not clinically relevant and is consistent with data from the literature.

Overall conclusions on pharmacokinetics

The bioequivalence studies supporting the claim of the test product to be a generic medicinal product of the reference product are of adequate design. The bioequivalence of the test and reference products was shown with 90% CI within the 0.8-1.25 and 0.7-1.43 acceptance limits for AUC and C_{max} respectively.

A separate bioequivalence study has not been carried out on the lower strength product and Marketing Authorisation applied for, Lansoprazole 15mg Gastro-Resistant Capsules (PL 04147/0052). This was not considered necessary as Lansoprazole 15mg Gastro-Resistant Capsules and Lansoprazole 30mg Gastro-Resistant Capsules meet the specified exemption criteria, as detailed in CPMP/EWP/QWP/1401/98. The results and conclusions of the bioequivalence studies submitted for the 30mg strength capsules were, therefore, extrapolated to the 15mg strength capsules, and we can conclude that the 15mg strength lansoprazole formulation is bioequivalent to its corresponding marketed brand formulation.

EFFICACY

Efficacy is reviewed in the Clinical Expert Report. The reference products are established and the applications depend upon the ability to demonstrate bioequivalence.

No new efficacy 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.

SAFETY

Safety is reviewed in the Clinical Expert Report.

No new safety data were submitted and none are required for these types of applications. The reference products are established and the main basis of the applications depends upon the bioequivalence study. The applicant has submitted a satisfactory literature review confirming the safety of lansoprazole capsules. No new safety issues have been detected.

EXPERT REPORT

A satisfactory expert report is provided, and has been prepared by an appropriately qualified expert. An appropriate CV for the expert has been supplied.

PRODUCT INFORMATION:

Summary of Product Characteristics

The approved SmPCs are consistent with those for the reference products and are acceptable.

Patient Information Leaflet

The PILs are in line with the approved SmPCs and are satisfactory.

Labelling

Colour mock-ups of the labelling have been provided. The labelling is satisfactory and fulfils the statutory requirements for Braille.

CONCLUSIONS

All issues have been adequately addressed by the applicant. The bioequivalence studies were of an appropriate design and bioequivalence of the 30mg strength test and reference products was shown with 90% Confidence Intervals within general acceptance limits. The conditions, as detailed in CPMP/EWP/QWP/1401/98, for bioequivalence studies for a single strength to cover multiple strengths of a product have been met, so the results and conclusions of the bioequivalence studies submitted for the 30mg strength capsules were extrapolated to the 15mg strength capsules. We can say, therefore, that the 15mg strength lansoprazole formulation is bioequivalent to its corresponding marketed brand formulation, despite bioequivalence not being assessed explicitly.

Sufficient clinical information has been submitted to support these applications. 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. Marketing Authorisations may be granted on medical grounds.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of Lansoprazole 15mg Gastro-Resistant Capsules and Lansoprazole 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 the reference product Agopton 30mg DR Capsules (Takeda Pharma GmbH), and consequently Zoton Capsules 30mg. As the test products were deemed to meet the criteria specified in the Note for Guidance on the investigation of bioavailability and bioequivalence (CPMP/EWP/QWP/1401/98), the results and conclusions of the bioequivalence studies on the 30mg strength were extrapolated to the 15mg capsule strength. Thus, no separate bioequivalence studies were necessary for this strength.

No new or unexpected safety concerns arise from these applications.

PRODUCT LITERATURE

The SmPCs, PILs and labelling are satisfactory and consistent with those for Zoton Capsules 15mg and Zoton Capsules 30mg.

The Marketing Authorisation Holder has provided a commitment to update the Marketing Authorisations with package leaflets in compliance with Article 59 of Council Directive 2001/83/EC and that the leaflets shall reflect the results of consultation with target patient groups, no later than 1st July 2008.

The approved labelling artwork complies with statutory requirements. In line with current legislation, the name of the product in Braille appears on the outer packaging and sufficient space has been included for a standard UK pharmacy dispensing label.

RISK BENEFIT ASSESSMENT

The quality of the products is acceptable and no new preclinical or clinical safety concerns have been identified. The bioequivalence studies, and the valid extrapolation of their results and conclusions, support the claim that the applicant's products and their respective reference products are interchangeable. 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. Extensive clinical experience is considered to have demonstrated the therapeutic value of the active substance. The risk: benefit is, therefore, considered to be positive.

LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES (LANSOPRAZOLE) PL 04147/0052

LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES (LANSOPRAZOLE) PL 04147/0053

STEPS TAKEN FOR ASSESSMENT

1 The MHRA received the marketing authorisation applications on 13th September 2004

2 Following standard checks and communication with the applicant the MHRA considered the applications valid on 23rd September 2004

3 Following assessment of the applications the MHRA requested further information relating to the clinical dossiers on 16th June 2005, and further information relating to the quality dossiers on 21st July 2005

4 The applicant responded to the MHRA's requests, providing further information for the clinical sections and the quality sections on 24th October 2005

5 Following assessment of the response the MHRA requested further information relating to the quality sections on 9th December 2005, 28th February 2006, 21st April 2006, 30th October 2006, 13th November 2006, and 15th January 2007

6 The applicant responded to the MHRA's request, providing further information for the quality sections on 20th December 2005, 21st April 2006, 27th August 2006, 13th November 2006, 3rd December 2006, and 19th April 2007 respectively

7 The applications were determined on 20th April 2007

SUMMARY OF PRODUCT CHARACTERISTICS

The UK Summary of Product Characteristics (SPC) for Lansoprazole 15mg Gastro-Resistant Capsules is as follows:

1 NAME OF THE MEDICINAL PRODUCT

Lansoprazole 15 mg Gastro-resistant Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 15 mg lansoprazole.

Excipients: Contains lactose

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Gastro resistant capsules, hard.

Opaque white hard gelatine capsules containing white or almost white, round gastroresistant microtablets. The upper part of the capsule is printed LP and the lower part is printed 15.

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.

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.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Dosage

Gastro Oesophageal Reflux Disease: 30 mg lansoprazole 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: 30 mg lansoprazole once daily for 4 weeks.

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

Acid-related dyspepsia: Intermittent courses, as required, of 15 mg or 30 mg lansoprazole 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: 30 mg lansoprazole once daily for 8 weeks.

Treatment of NSAID-associated benign gastric and duodenal ulcers and relief of symptoms: 15 mg or 30 mg lansoprazole 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: 15 mg or 30 mg lansoprazole once daily.

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

For patients who require 120 mg or more per day, the dose should be divided and administered twice daily. To achieve the optimal acid inhibitory effect, and hence the 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.

4.3 CONTRAINDICATIONS

Known hypersensitivity to lansoprazole or any of the excipients.

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.

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 30 mg 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*.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 INTERACTION 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 and should, therefore, not be taken within an hour of 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 pruritis. 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 inhibitor

ATC CODE: A02B C03

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 (proto 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 30 mg inhibits pentagastrin-stimulated acid secretion by approximately 80%, indicating effective acid inhibition from the first day of dosing.

Lansoprazole has a prolonged pharmacological action providing effective acid suppression over 24 hours, thereby promoting rapid healing and symptom relief.

By reducing gastric acidity, lansoprazole creates an environment in which appropriate antibiotics can be effective against *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. 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 tablets:

Lactose monohydrate,

hypromellose,

crospovidone,

glycerol dibehenate,

titanium dioxide,

silicon dioxide,

talc,

triethylcitrate,

methacrylic acid copolymer.

Capsule shell:

Gelatin,

titanium dioxide,

black ink TEK SW-9008(contains black iron oxide E172).

6.2 INCOMPATIBILITIES

Not applicable.

6.3 SHELF LIFE

18 months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Do not store above 25^{o}C. Store in the original container.

6.5 NATURE AND CONTENTS OF CONTAINER

HDPE bottle with desiccant containing 50 capsules or aluminium blisters containing 28 or 56 capsules.

Not all pack sizes may be marketed.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Medo Pharmaceuticals Limited
East Street
Chesham
Bucks, HP5 1DG
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 04147/0052

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

20/04/2007

10 DATE OF REVISION OF THE TEXT

20/04/2007

SUMMARY OF PRODUCT CHARACTERISTICS

The UK Summary of Product Characteristics (SPC) for Lansoprazole 30mg Gastro-Resistant Capsules is as follows:

1 NAME OF THE MEDICINAL PRODUCT

Lansoprazole 30 mg Gastro-resistant Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 30 mg lansoprazole.

Excipients: Contains lactose

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Gastro resistant capsules, hard

Opaque white hard gelatine capsules containing white or almost white, round gastroresistant microtablets. The upper part of the capsule is printed LP and the lower part is printed 30.

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.

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.

4.2 POSOLOGY AND METHOD OF ADMINISTRATION

Dosage

Gastro Oesophageal Reflux Disease: 30 mg lansoprazole 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: 30 mg lansoprazole once daily for 4 weeks.

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

Acid-related dyspepsia: Intermittent courses, as required, of 15 mg or 30 mg lansoprazole 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: 30 mg lansoprazole once daily for 8 weeks.

Treatment of NSAID-associated benign gastric and duodenal ulcers and relief of symptoms: 15 mg or 30 mg lansoprazole 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: 15 mg or 30 mg lansoprazole once daily.

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

For patients who require 120 mg or more per day, the dose should be divided and administered twice daily. To achieve the optimal acid inhibitory effect, and hence the 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.

4.3 CONTRAINDICATIONS

Known hypersensitivity to lansoprazole or any of the excipients.

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.

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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*.

Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 INTERACTION 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.

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Antacids and sucralfate may reduce the bioavailability of lansoprazole and should, therefore, not be taken within an hour of lansoprazole.

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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.

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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 pruritis. 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 ahs 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

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Pharmacotherapeutic group: Proton pump inhibitor

ATC CODE: A02B C03

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 (proto 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 30 mg inhibits pentagastrin-stimulated acid secretion by approximately 80%, indicating effective acid inhibition from the first day of dosing.

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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. 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 tablets:

Lactose monohydrate,

hypromellose,

crospovidone,

glycerol dibehenate,

titanium dioxide,

silicon dioxide,

talc,

triethylcitrate,

methacrylic acid copolymer.

Capsule shell:

Gelatin,

titanium dioxide,

black ink TEK SW-9008(contains black iron oxide E172).

6.2 INCOMPATIBILITIES

Not applicable.

6.3 SHELF LIFE

HDPE bottles: 24 months

Aluminium blisters: 18 months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Do not store above 25^{o}C. Store in the original container.

6.5 NATURE AND CONTENTS OF CONTAINER

HDPE bottle with desiccant containing 50 capsules or aluminium blisters containing 7, 14, 28, 42 or 56 capsules.

Not all pack sizes may be marketed.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

Not applicable.

7 MARKETING AUTHORISATION HOLDER

Medo Pharmaceuticals Limited
East Street
Chesham
Bucks, HP5 1DG
UK

8 MARKETING AUTHORISATION NUMBER(S)

PL 04147/0053

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

20/04/2007

10 DATE OF REVISION OF THE TEXT

20/04/2007

PATIENT INFORMATION LEAFLET

Lansoprazole 15mg Gastro-Resistant Capsules

lansoprazole 15 mg

gastro-resistant capsules

LANSOPRAZOLE 15 mg

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 your 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:

1. WHAT ARE LANSOPRAZOLE CAPSULES AND WHAT ARE THEY USED FOR

Lansoprazole capsules are hard gelatin capsules that contain white or almost white gastro-resistant tablets. They are available in two strengths. The capsules are printed '15' on one half and the other half contains 15 mg of the active ingredient lansoprazole.

The capsules also contain: lactose monohydrate, hypromellose, crospovidone, glycerol dibehenate, titanium dioxide, silicon dioxide, talc, triethylcitrate, methacrylic acid copolymer, gelatin, black ink TEK SW-9008 (contains black iron oxide E172).

Lansoprazole belongs to a group of medicines called proton pump inhibitors. It reduces the amount of acid that your stomach makes.

Lansoprazole 15 mg Capsules are available in blister packs containing 28 or 56 capsules, or bottles containing 50 capsules. Not all pack sizes may be marketed.

The Marketing Authorisation Holder is Medo Pharmaceuticals Limited.
The product is manufactured by Medinsa Laboratorios Medicamentos Internacionales S.A., Solana 26, 28 850 Torrejon de Ardoz, Madrid.

Your doctor has prescribed Lansoprazole Capsules in order to treat one of the following:

- If you have a damaged or inflamed oesophagus (Gastro-Oesophageal Reflux Disease – GORD)
- If you have a duodenal or stomach ulcer
- If you have heartburn or indigestion as a result of the condition called acid-related dyspepsia
- If you have an ulcer as a result of taking NSAIDs
- If your stomach produces too much acid (Zollinger-Ellison syndrome)

Lansoprazole Capsules may also be prescribed in order to prevent these conditions returning.

2. BEFORE YOU TAKE LANSOPRAZOLE CAPSULES

Do not take Lansoprazole Capsules:

- if you are allergic to lansoprazole or any of the other ingredients of Lansoprazole Capsules

Take special care with Lansoprazole Capsules:

- if you have liver problems. You may still be able to take the capsules but your doctor may reduce the dose.

Pregnancy

You should not take Lansoprazole Capsules if you are pregnant or you think you may be pregnant.

Breast-feeding

You should not take Lansoprazole Capsules if you are breast-feeding.

Important information about some of the ingredients of Lansoprazole Capsules:

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

Taking other medicines:

Tell your doctor is you are taking any of the following medicines:

- The contraceptive pill
- Phenytoin or carbazepine, medicines used for epilepsy

– Theophylline, a medicine used for asthma
– Warfarin, a medicine used to thin the blood
– Antacids or sucralfate, medicines used to treat indigestion

Please inform your doctor or pharmacist if you are taking or have recently taken any other medicines, even those not prescribed.

3. HOW TO TAKE LANSOPRAZOLE CAPSULES

Always take Lansoprazole Capsules exactly as your doctor has instructed you. You should check with your doctor or pharmacist if you are unsure. The capsules should be swallowed whole. Do not crush or chew.

The dose prescribed by your doctor will depend on your medical condition. The usual dose is 15 - 30 mg lansoprazole a day for between 4 to 8 weeks. Your doctor will normally prescribe a dose of 60 mg or more a day if you have Zollinger-Ellison syndrome. If you have liver problems then your doctor will prescribe you a lower dose.

For the most effective relief from symptoms, take one capsule in the morning before breakfast. If your doctor has advised you to take two capsules per day, take the second capsule in the evening.

Lansoprazole Capsules should not be taken by children.

If you take more Lansoprazole Capsules than you should: Inform your doctor or pharmacist immediately.

If you forget to take Lansoprazole Capsules: Take your dose as soon as you remember unless it is nearly time for your next dose. In this case, skip the missed dose and take the rest of your capsules as usual. Do not take a double dose.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Lansoprazole Capsules can have side effects. These are usually mild and do not last for a long time.

If any of the following happen, stop taking Lansoprazole Capsules and tell your doctor immediately or go to the casualty department at your nearest hospital:
– Facial swelling
– Shortness of breath or difficulty breathing
– Skin rash or blistering of the skin
– Yellowing of the skin and eyes
– Bruising

All of these very serious side effects are very rare.

Other rare side effects include: kidney problems, inflammation of the liver (hepatitis) or changes in kidney or liver function.

Very rarely you may experience severe diarrhoea. If you do, see your doctor as soon as possible as you may need to stop taking the capsules.

Other possible side effects are headache, dizziness, feeling tired or unwell, diarrhoea, constipation, stomach pain, feeling and/or being sick, wind, dry or sore mouth and throat, itchy skin, thinning of the hair, sensitivity to light, muscle or joint pain, depression, swelling, pins and needles sensation, blurred vision, taste disturbances, vertigo, confusion and hallucinations.

Rarely men may experience impotence or breast swelling.

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

5. STORING LANSOPRAZOLE CAPSULES

Keep out of the reach and sight of children.

Do not store above 25°C

Store in the original container

Do not use after the expiry date stated on the packaging.

Date of preparation: August 2006.

Lansoprazole 30mg Gastro-Resistant Capsules

lansoprazole 30 mg

gastro-resistant capsules

LANSOPRAZOLE 30 mg

Patient information leaflet

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

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- 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.

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The capsules also contain: lactose monohydrate, hypromellose, crospovidone, glycerol dibehenate, titanium dioxide, silicon dioxide, talc, triethylcitrate, methacrylic acid copolymer, gelatin, black ink TEK SW-9008 (contains black iron oxide E172).

Lansoprazole belongs to a group of medicines called proton pump inhibitors. It reduces the amount of acid that your stomach makes.

Lansoprazole 30 mg Capsules are available in blister packs containing 7, 14, 28, 42 or 56 capsules, or bottles containing 50 capsules. Not all pack sizes may be marketed.

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The product is manufactured by Medinsa Laboratorios Medicamentos Internacionales S.A., Solana 26, 28 850 Torrejon de Ardoz, Madrid.

Your doctor has prescribed Lansoprazole Capsules in order to treat one of the following:

- If you have a damaged or inflamed oesophagus (Gastro-Oesophageal Reflux Disease – GORD)
- If you have a duodenal or stomach ulcer
- If you have heartburn or indigestion as a result of the condition called acid-related dyspepsia
- If you have an ulcer as a result of taking NSAIDs
- If your stomach produces too much acid (Zollinger-Ellison syndrome)

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- if you are allergic to lansoprazole or any of the other ingredients of Lansoprazole Capsules

Take special care with Lansoprazole Capsules:

- if you have liver problems. You may still be able to take the capsules but your doctor may reduce the dose.

Pregnancy

You should not take Lansoprazole Capsules if you are pregnant or you think you may be pregnant.

Breast-feeding

You should not take Lansoprazole Capsules if you are breast-feeding.

Important information about some of the ingredients of Lansoprazole Capsules:

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

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Tell your doctor is you are taking any of the following medicines:

- The contraceptive pill
- Phenytoin or carbazepine, medicines used for epilepsy

– Theophylline, a medicine used for asthma
– Warfarin, a medicine used to thin the blood
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Please inform your doctor or pharmacist if you are taking or have recently taken any other medicines, even those not prescribed.

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The dose prescribed by your doctor will depend on your medical condition. The usual dose is 15 - 30 mg lansoprazole a day for between 4 to 8 weeks. Your doctor will normally prescribe a dose of 60 mg or more a day if you have Zollinger-Ellison syndrome. If you have liver problems then your doctor will prescribe you a lower dose.

For the most effective relief from symptoms, take one capsule in the morning before breakfast. If your doctor has advised you to take two capsules per day, take the second capsule in the evening.

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If you take more Lansoprazole Capsules than you should: Inform your doctor or pharmacist immediately.

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– Bruising

All of these very serious side effects are very rare.

Other rare side effects include: kidney problems, inflammation of the liver (hepatitis) or changes in kidney or liver function.

Very rarely you may experience severe diarrhoea. If you do, see your doctor as soon as possible as you may need to stop taking the capsules.

Other possible side effects are headache, dizziness, feeling tired or unwell, diarrhoea, constipation, stomach pain, feeling and/or being sick, wind, dry or sore mouth and throat, itchy skin, thinning of the hair, sensitivity to light, muscle or joint pain, depression, swelling, pins and needles sensation, blurred vision, taste disturbances, vertigo, confusion and hallucinations.

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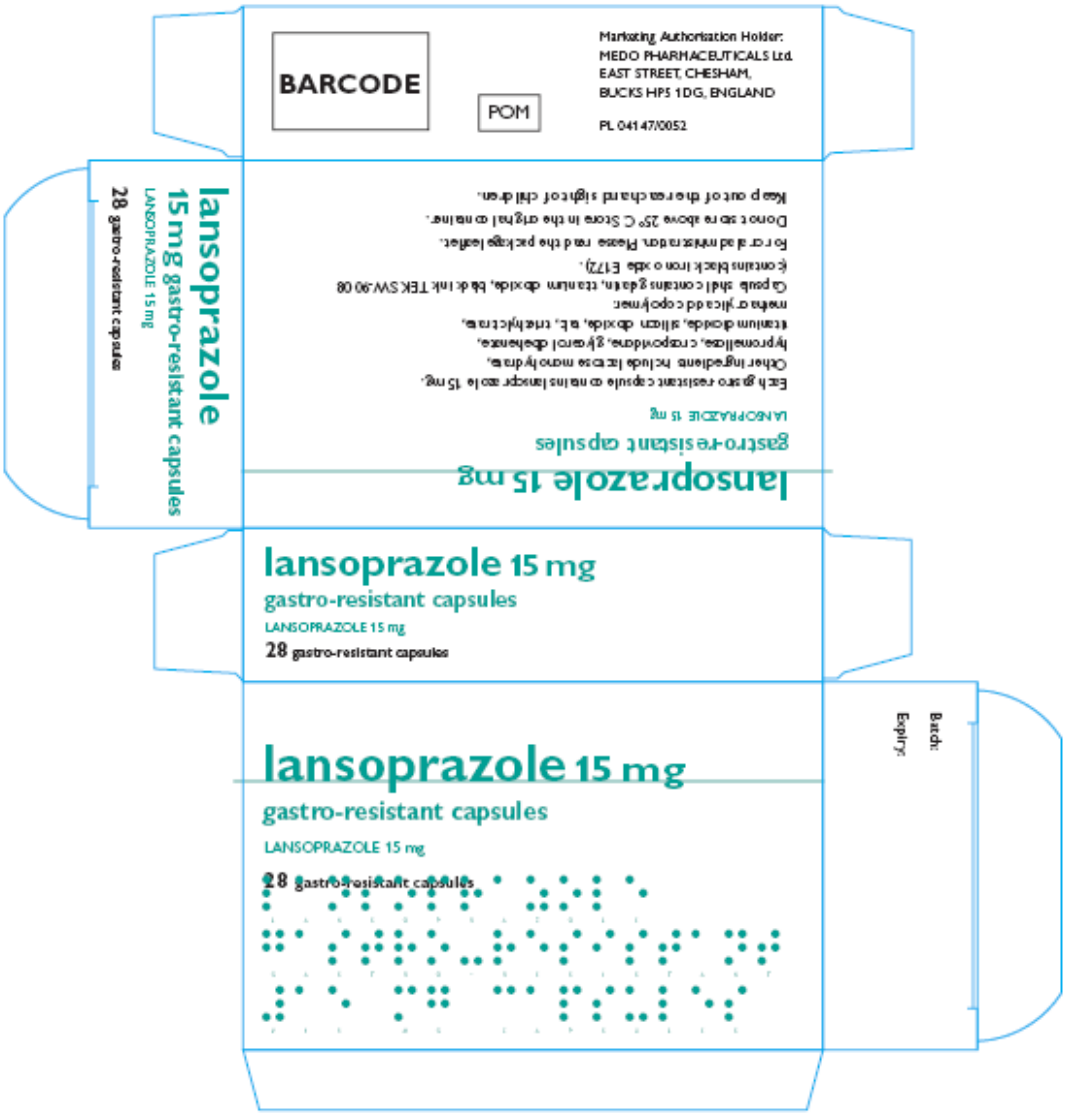
Do not store above 25°C

Store in the original container

Do not use after the expiry date stated on the packaging.

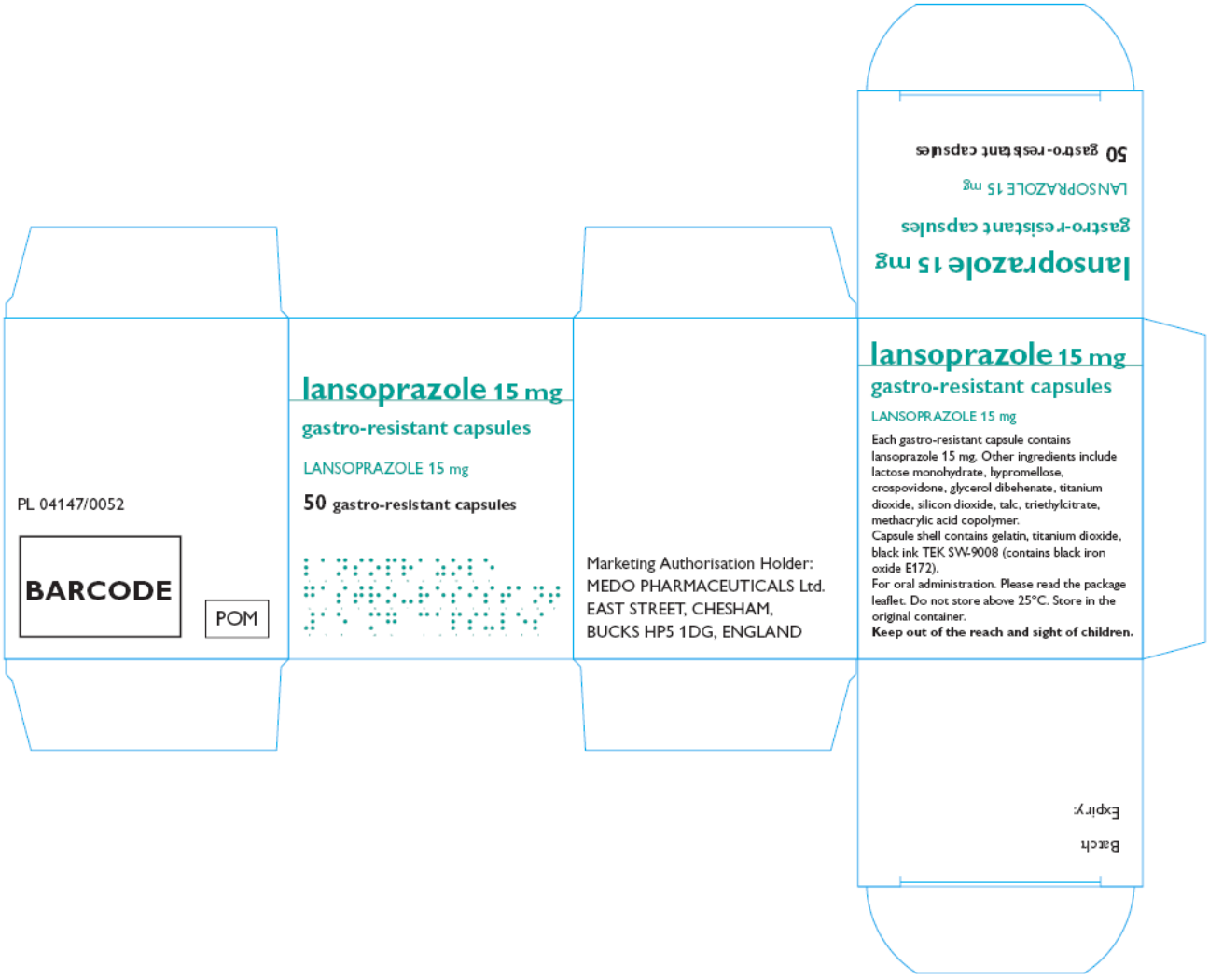
Date of preparation: August 2006.

LABELLING
Lansoprazole 15mg Gastro-Resistant Capsules
Carton for blisters, with braille



Blister foil

Carton for HDPE bottle, with braille



HDPE Bottle label

Batch number:

Expiry date:

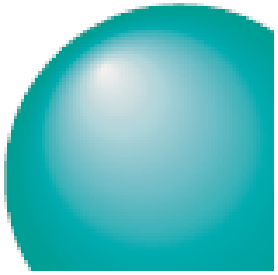
lansoprazole 15mg

gastro-resistant capsules

LANSOPRAZOLE 15 mg

50 gastro-resistant capsules

MEDO PHARMACEUTICALS Ltd.
EAST STREET, CHESHAM
BUCKS, HP5 1DG, ENGLAND



Each capsule contains lansoprazole 15 mg. Other ingredients include lactose monohydrate, hypromellose, crospovidone, glycerol dibehenate, titanium dioxide, silicon dioxide, talc, triethylcitrate methylic acid copolymer. Capsule shell contains gelatin, titanium dioxide, black ink TEK SW-9008 (contains black iron oxide E172)

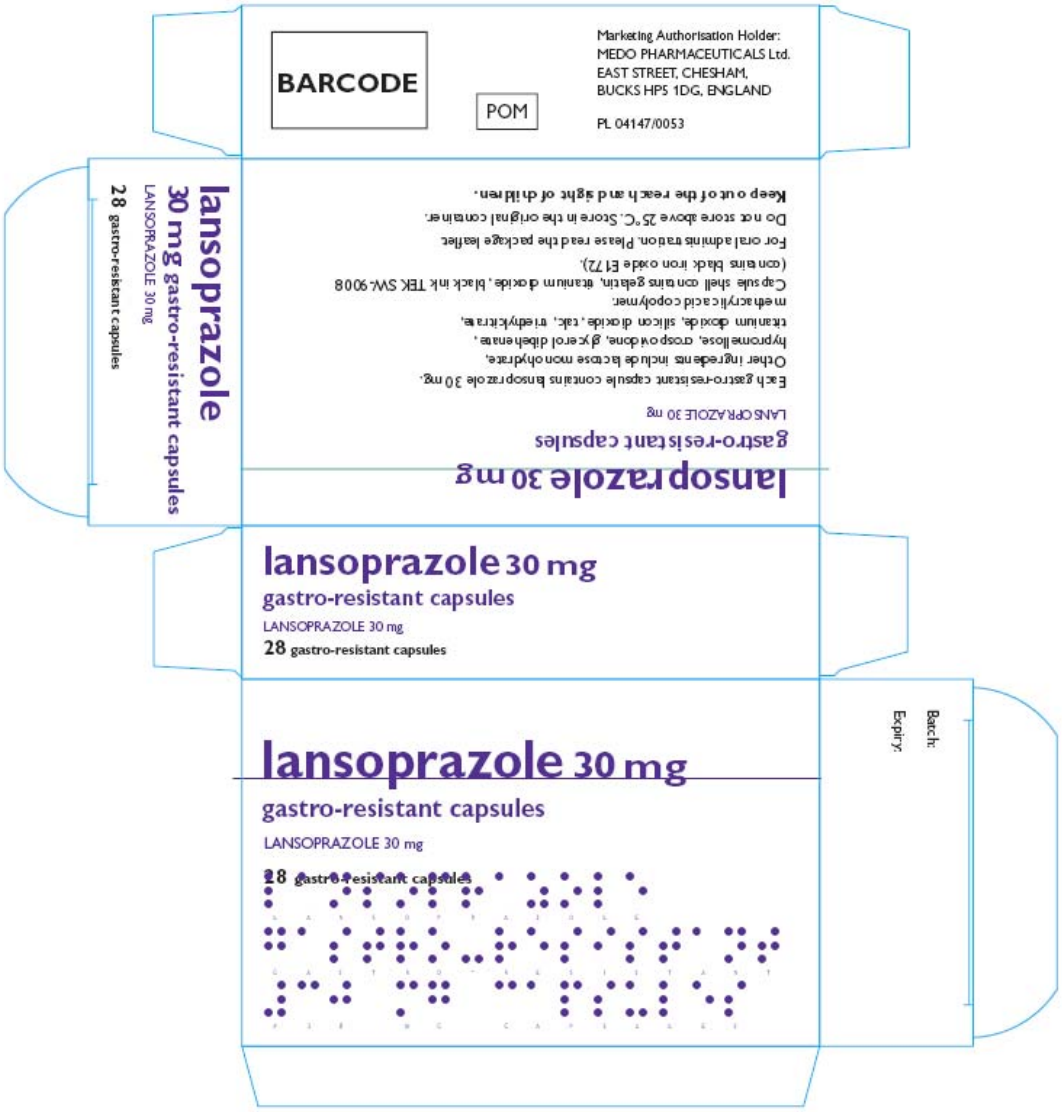
For oral administration. Please read the package leaflet. Do not store above 25°C. Store in the original container.

Keep out of the reach and sight of children.

PL 04147/0052

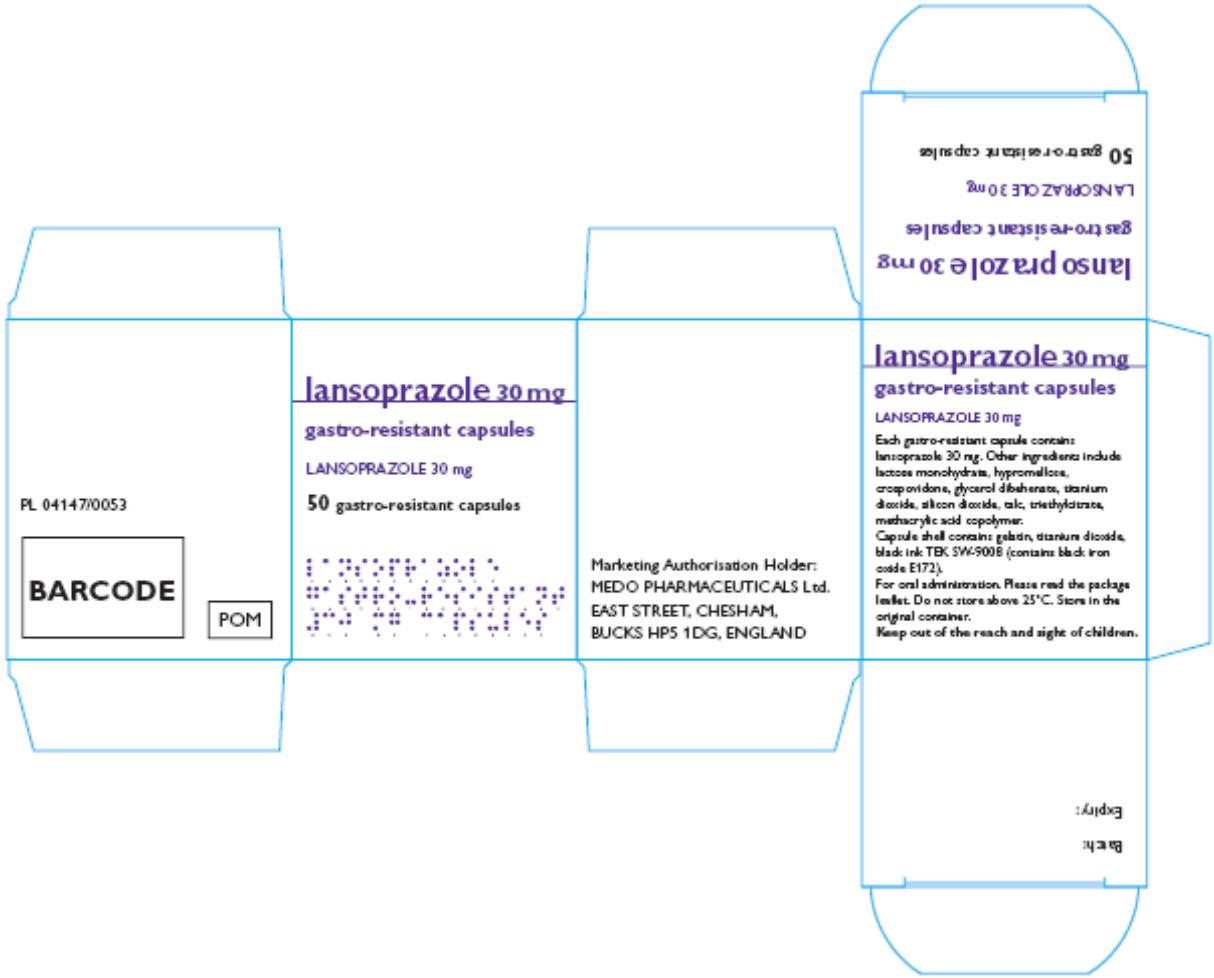
POM

Lansoprazole 30mg gastro-resistant capsules
Carton for blisters, with braille



Blister foil

Carton for HDPE bottle, with braille



HDPE Bottle label

Batch number:

Expiry date:

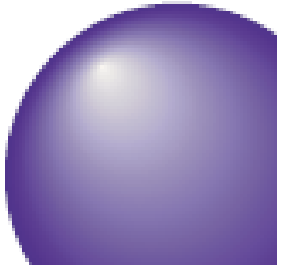
lansoprazole 30mg

gastro-resistant capsules

LANSOPRAZOLE 30 mg

50 gastro-resistant capsules

MEDO PHARMACEUTICALS Ltd.
EAST STREET, CHESHAM
BUCKS, HP5 1DG, ENGLAND



Each capsule contains lansoprazole 30 mg. Other ingredients include lactose monohydrate, hypromellose, crospovidone, glycerol dibehenate, titanium dioxide, silicon dioxide, talc, triethylcitrate methylic acid copolymer. Capsule shell contains gelatin, titanium dioxide, black ink TEK SW-9008 (contains black iron oxide E172)

For oral administration. Please read the package leaflet. Do not store above 25°C. Store in the original container.

Keep out of the reach and sight of children.

PL 04147/0053

POM