LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 08608/0120, 0122, 0124 and 0126

LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0121, 0123, 0125 and 0127

UKPAR

TABLE OF CONTENTS

LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 08608/0120, 0122, 0124 and 0126

LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0121, 0123, 0125 and 0127

LAY SUMMARY

The MHRA today granted Olinka (UK) Limited Marketing Authorisations (licences) for the medicinal products Lansoprazole 15mg Gastro-Resistant Capsules (PL 08608/0120, 0122, 0124 and 0126) and Lansoprazole 30mg Gastro-Resistant Capsules (PL 08608/0121, 0123, 0125 and 0127). 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 the amount of acid the stomach makes.

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 08608/0120, 0122, 0124 and 0126

LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0121, 0123, 0125 and 0127

SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

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 (and duplicates) to Olinka (UK) Limited (PL 08608/0120-127) on 4th August 2007. 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 Zoton 15mg and 30mg Capsules (originally granted to Cyanamid of Great Britain Limited in 1996 and 1994, respectively).

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 one of the class of 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 as an adjuvant in the eradication of *H. pylori*.

For these particular generic products, the applicant requested that indications and advice related to the treatment of *H pylori* be removed from the product literature due to concerns related to patent protection. These parts of the license 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 bioequivalence study comparing the applicant's 30mg product with the Opiren 30mg Capsules (Almirall Prodesfarma, Spain). Consequently, all sections of this Scientific Discussion refer to both products.

PHARMACEUTICAL ASSESSMENT

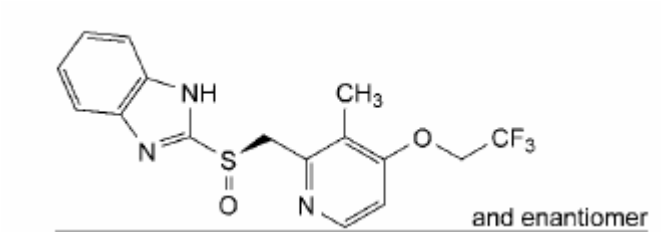
DRUG SUBSTANCE

INN: Lansoprazole

Chemical Name: 2-[[[3-methyl-4-(2, 2, 2-trifluoroethoxy)- pyridine-2-yl]methyl]sulfinyl benzimidazole

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

Structure:



Molecular Weight: 369.37

Appearance: White to off-white crystalline 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 BP or Ph Eur, but a USP monograph is available.

Synthesis of the drug substance from the designated starting materials 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.

All potential known impurities have been identified and characterised. Appropriate proof of structure has been supplied for the active pharmaceutical ingredient.

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.

The drug substance is packaged in double polyethylene bags that are tied with a plastic cable and contained in drums. The immediate packaging complies with EEC requirements for materials suitable for contact with food.

Appropriate stability data have been provided to support a retest period of 24 months when stored at 2-8°C in the proposed packaging. A post approval commitment to place one batch of active on long-term stability annually has been provided.

DRUG PRODUCT

Pharmaceutical Development

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

The rationale and function of each excipient added is discussed. Levels of each ingredient are typical for a product of this nature. Other ingredients consist of sugar spheres, sodium starch glycollate (type A), sodium lauril sulfate, Povidone K30, potassium oleate, oleic acid, Hypromellose, methacrylic acid-ethyl acrylate co-polymer, triethyl citrate, titanium dioxide, talc and gelatin shell (consisting of titanium dioxide purified water and gelatin) and printing ink (consisting of shellac -lacca, propylene glycol, ammonium hydroxide, potassium hydroxide and black iron oxide E172).

All excipients used in the capsule fill, gelatine capsules and printing ink comply with a suitable specification.

Gelatin used in the manufacture of the capsules is the only material of animal or human origin used. Satisfactory Certificates of Suitability have been provided to show compliance with current legislation to minimise TSE infection.

Comparative *in vitro* dissolution profiles have been generated for the proposed products and Opiren 15mg and 30mg Capsules with satisfactory results.

Comparative assay and impurity profiles have been generated for Zoton Capsules, Opiren Capsules and test products. The data provided shows that test and reference products can be considered essentially similar in terms of impurity levels.

Manufacture

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. A commitment has been given to fully validate the encapsulation process up to the proposed batch size.

Control of Drug Product

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 and stability data have demonstrated compliance with the proposed release and shelf-life specification.

Satisfactory data on the characterisation of impurities have been provided. All known impurities for the finished product are the same as those for the active ingredient.

Reference Standards or Materials
Satisfactory details have been provided for active lansoprazole and impurity reference standards.

Container Closure System
Both capsule strengths are packaged in HDPE bottles with a PP cap (with integral silica gel desiccant). Satisfactory specifications and certificates of analysis have been provided for the packaging components. Pack sizes are 7, 14, 28 and 56 capsules (2 x 28 capsules).

Stability of the Drug Product
Stability data provided support a shelf-life of 24 months for both strengths, with the storage conditions: 'Do not store above 30°C. Store in the original package. Keep the bottle tightly closed to protect from moisture'.

Bioequivalence/bioavailability
Satisfactory Certificates of Analysis have been provided for the test and reference batches used in the bioequivalence study. Bio-analytical methods used have been satisfactorily validated.

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, pharmaceutical form and bioequivalence.

PRECLINICAL ASSESSMENT

In these applications, essential similarity is being claimed between these generic products and Zoton 15mg and 30mg Capsules, which have been licensed within the EEA for over 10 years.

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

CLINICAL ASSESSMENT

INTRODUCTION

These are national abridged applications for generic equivalents of lansoprazole 15 and 30 mg capsules which have been licensed in the UK for over 10 years

The applicant requested that indications and advice related to the treatment of *H pylori* be removed from the product literature due to concerns related to patent protection. These parts of the license are therefore dissimilar to those of the reference product.

CLINICAL PHARMACOLOGY

Pharmacodynamics

Lansoprazole is a proton pump inhibitors, inhibiting specifically the H+ / K+ ATPase (proton pump) of the parietal cell in the stomach, the terminal step in acid production. Reduced gastric acidity is 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.

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.

Pharmacokinetics

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 14C-labelled lansoprazole indicated that up to 50% of the dose was excreted in the urine. Lansoprazole is metabolised substantially by the liver.

Bioequivalence

LAN-2003/006. Bioequivalence in fasting and after breakfast conditions, of two lansoprazole formulations (30mg capsules after multiple doses, by oral route in healthy volunteers.

Centre: Conducted at the Unit of Clinical Pharmacology Studies of the Hospital Clinico San Carlos by the principle investigator, Dr A Portoles.

The study complied with GCP, ICH guidelines, the recommendations of the WHO and the Declaration of Helsinki.

Design: Randomised, open-label, crossover study separated by a 7-day washout. Blood sampling was performed on Day 6 (under fasting conditions) and on Day 7 (non-fasting conditions).

Results: **Summary of main pharmacokinetic parameters of lansoprazole (Fasting) - N=24**

Parameter	**Values**			
	Mean +/- SD (range)		**Ratio**	**90% CI**
	Opiren	**Belmac lansoprazole**		
AUC_{last}	3299.0 +/- 2451.4	3330.1 +/- 2458.7	102.54	88.96 to 118.20
(ng.h/ml)	(513.5 – 10458.6)	(852.8 – 10303.0)		
AUC_{inf}	3483.9 +/- 2877.7	3525.2 +/- 2904.1	102.33	89.57 to 116.91
(ng.h/ml)	(587.0 – 12004.4)	863.8 – 12264.2)		
C_{max}	1080.4 +/- 482.0	1035.4 +/- 464.5	96.79	80.13 to 116.92
(ng/ml)	(132.5 – 2300.7)	(158.5 – 2151.9)		
T_{max}	1.84 +/- 0.66(45)	2.32 +/- 1.19)	-	-
(h)	(1.00 – 3.97)	1.00 – 6.00		

Summary of main pharmacokinetic parameters of lansoprazole (Fed) - N=24

Parameter	**Values**			
	Mean +/- SD (range)		**Ratio**	**90% CI**
	Opiren	**Belmac lansoprazole**		
AUC_{last}	3098.6 +/- 1788.7	3013.6 +/- 2011.7		
(ng.h/ml)	(907.4 – 8783.3)	(669.8 – 9324.1)	94.84	86.16 to 104.39
AUC_{inf}	3299.2 +/- 2229.0	3527.4 +/- 2658.9	102.83	91.83 to 115.4
(ng.h/ml)	1053.08(92)	(725.8 – 11247.4)		
C_{max}	892.1 +/- 367.1	761.7 +/- 370.9	82.34	69.87 to 97.03
(ng/ml)	(298.6 – 1944.3)	(159.8 – 1833.7)		
T_{max}	3.13 +/- 1.15	5.07 +/- 1.54)	-	-
(h)	(1.67 – 6.00)	(1.33 – 8.00)		

Conclusions: Under fasting conditions, the test and reference products were considered to be bioequivalent. It was considered acceptable to test the higher strength only since the pharmacokinetics of lansoprazole are said to be linear between the 15 and 60 mg range. The reference product is stated to be identical to the UK brand leader

Under non-fasting conditions, the AUC parameters were supportive for bioequivalence of the test and reference products. The C_{max} was outside the customary range, but considered acceptable being less clinically significant than the main

parameter, the AUC. Additionally it is recommended that lansoprazole is taken before breakfast when administered once daily.

In practice the ideal conditions for taking lansoprazole are thought to be on an empty stomach (when bioavailability will be maximal). However, food should be consumed within an hour or so after, as inhibition of acid secretion is thought to be optimal when the gastric cell proton pump has been stimulated. Studies where food is delayed by several hours after the administration of lansoprazole show less acid inhibition.

EFFICACY

No new data are required and the literature review included in the application confirms the effectiveness of lansoprazole capsules.

SAFETY

No new data are needed. A summary of safety from the world literature has been provided and the clinical expert confirms that no new safety issues have been detected.

EXPERT REPORT

A satisfactory clinical expert report has been submitted, which has been written by an appropriately qualified medical practitioner.

SUMMARY OF PRODUCT CHARACTERISTICS

This is satisfactory and consistent with those for the reference products.

PATIENT INFORMATION LEAFLET

This is satisfactory and consistent with the SPC.

LABELLING

These have been approved.

DISCUSSION

Proton pump inhibitors, including lansoprazole, have been available in the UK for well over 10 years. Their use is well-established with recognised efficacy and acceptable safety.

With regard to the current applications, there has been no requirement for new clinical efficacy or safety data, but a satisfactory literature review has been included.

The products are considered to be within the acceptable bioequivalence range as the reference products. When used as indicated, lansoprazole has a favourable benefit-to-risk ratio

CONCLUSION

Overall, there are no clinical objections to the grant of marketing authorisations for these applications. No new or unexpected safety concerns arise from these applications. The SPC, PIL and packaging are satisfactory and consistent with that for the reference product.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

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

PRECLINICAL

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

EFFICACY

Bioequivalence has been demonstrated between the applicant's Lansoprazole 30mg Capsules and Zoton 30mg Capsules (originally granted to Cyanamid of Great Britain Limited). 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, PIL and labelling are satisfactory and consistent with that for the reference products, with the exception of text relating to the treatment of *H pylori* infection for the reasons given above.

RISK BENEFIT ASSESSMENT

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

LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 08608/0120, 0122, 0124 and 0126

LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0121, 0123, 0125 and 0127

STEPS TAKEN FOR ASSESMENT

1	The MHRA received the marketing authorisation applications on 24th March 2005
2	Following standard checks and communication with the applicant the MHRA considered the applications valid on 14th April 2005
3	Following assessment of the applications the MHRA requested further information relating to the quality and clinical dossiers.
4	The applicant responded to the MHRA's requests, providing further information during 2005-2007 with proposals for the final product literature in July 2007.
5	The applications were determined on 3rd August 2007

LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 08608/0120, 0122, 0124 and 0126

LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0121, 0123, 0125 and 0127

STEPS TAKEN AFTER AUTHORISATION - SUMMARY

Date submitted	Application type	Scope	Outcome

1 NAME OF THE MEDICINAL PRODUCT

Lansoprazole 15 mg Gastro-resistant Capsules.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains lansoprazole, 15 mg

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Gastro-resistant capsule, hard.
Size 3, white cap marked with 'L' and white body marked with '15', containing white to beige gastro-resistant micropellets.

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 H2 receptor antagonists.

4.2 Posology and method of administration

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

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

Acid-related dyspepsia: Intermittent courses, as required, of Lansoprazole 15 mg or 30 mg once daily for 2-4 weeks depending on the severity and persistence of symptoms. Patients who do not respond after 4 weeks, or who relapse shortly afterwards, should be investigated.

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

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

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

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

Hypersecretory conditions: The initial dose should be lansoprazole 60mg 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 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

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.

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

4.5 Interaction with other medicinal products and other forms of interaction

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.

Pregnancy and lactation

For lansoprazole no clinical data on exposed pregnancies are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonic/foetal development, parturition or postnatal development.

The use of lansoprazole during pregnancy is not recommended.

It is not known whether lansoprazole is excreted in human breast milk. Animal studies have shown excretion of lansoprazole in milk. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with lansoprazole should be made taking into account the benefit of breast-feeding to the child and the benefit of lansoprazole therapy to the woman.

The use of lansoprazole during breast feeding should be avoided unless considered essential.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

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

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

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

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

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

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

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

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

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

Gynaecomastia and impotence have been reported rarely.

4.9 Overdose

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

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

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.

5.2 Pharmacokinetic properties

Absorption

Lansoprazole is rapidly inactivated by gastric acid. Therefore it is formulated as enteric-coated granules in gelatin capsules. Lansoprazole is rapidly absorbed from the duodenum; peak plasma concentrations are achieved within 1.5 – 2.0 hours. Intake of food slows the absorption rate and reduces its bioavailability (AUC) by approximately 25%.

Distribution

The bioavailability after a single lansoprazole 30 mg dose and after repeated daily administration is 80 – 90%. The bioavailability of lansoprazole may be reduced if antacids and sucralfate are co-administered. Plasma protein binding is approximately 95%. This has no significant effect on other protein bound active substances.

Metabolism

Lansoprazole is mainly metabolised in the liver.

Lansoprazole is mainly catalysed by the enzyme CYP 2C19. CYP 3A4 also contributes to the metabolism of lansoprazole. CYP 2C19 is subject to genetic polymorphism and approximately 2 – 65 of the general population are termed poor metabolisers (PMs) who are homozygote for a mutant CYP 2C19 allele. PMs lack a functional CYP 2C19 enzyme. In these PMs, exposure of lansoprazole is several-fold higher than in extensive metabolisers.

Three metabolites have been identified in the plasma: the sulfone, 5-hydroxy lansoprazole and the sulfide. These metabolites have a negligible effect on acid secretion.

Excretion
The elimination half-life of lansoprazole is 1.0 – 2.0 hours. Half life is not changed during repeated dosing of lansoprazole. A single dose of lansoprazole has an inhibitory effect on gastric acid secretion, which lasts for more than 24 hours. Since lansoprazole is activated in the parietal cells, its plasma concentration is not related to gastric acid secretion. Approximately, 15 – 50% of the metabolites are excreted in the urine and the remainder in the faeces. Three metabolites have been identified in the urine namely: 5-hydroxy sulfone, 5-hydroxy sulphide and 5-hydroxy lansoprazole.

In patients with cirrhosis, the AUC of lansoprazole is significantly increased and the elimination half life is prolonged; however, no signs of accumulation have been detected. The bioavailability of lansoprazole is not significantly changed in patients with renal insufficiency.

In the elderly, elimination of lansoprazole is slightly delayed.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, toxicity to reproduction or genotoxicity.

In two rat carcinogenicity studies, lansoprazole produced dose-related gastric ECL cell hyperplasia and ECL cell carcinoids associated with hypergastrinaemia due to inhibition of acid secretion. Intestinal metaplasia was also observed, as were Leydig cell hyperplasia and benign Leydig cell tumours. After 18 months of treatment retinal atrophy was observed. This was not seen in monkeys, dogs or mice.

In mouse carcinogenicity studies dose-related gastric ECL cell hyperplasia developed as well as liver tumours and adenoma of rete testis.

The clinical relevance of these findings is unknown.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule Content:
Sugar spheres (sucrose and maize starch)
Sodium starch glycolate Type A
Sodium laurilsulfate
Povidone K30
Potassium oleate
Oleic acid
Hypromellose
Methacrylic acid - ethyl acrylate copolymer 1:1
Triethyl citrate
Titanium dioxide (E171)
Talc

Body Composition:
Titanium dioxide (E171)
Gelatin

Cap Composition:
Titanium dioxide (E171)
Gelatin (Limited Bone Gelatin)
Water

Printing Ink:
Shellac (Lacca)
Propylene glycol
Ammonium hydroxide
Potassium hydroxide
Black iron oxide (E172)

6.2 Incompatibilities
Not applicable

6.3 Shelf life
2 years.

6.4 Special precautions for storage
Do not store above 30ºC. Store in the original package. Keep the bottle tightly closed to protect from moisture.

6.5 Nature and contents of container
HDPE bottle, polypropylene cap with integral silica gel desiccant

Packs of 7, 14, 28 or 56 capsules (2 x 28 capsules)
Not all pack sizes are marketed.

6.6 Special precautions for disposal
No special instructions

7 MARKETING AUTHORISATION HOLDER
Olinka (UK) Limited,
38/40 Chamberlayne Rd.,
London NW10 3JE,
United Kingdom.

8 MARKETING AUTHORISATION NUMBER(S)
PL 08608/0120, 0122, 0124, 0126

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
03/08/2007

10 DATE OF REVISION OF THE TEXT
03/08/2007

1 NAME OF THE MEDICINAL PRODUCT

Lansoprazole 30 mg Gastro-resistant Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains lansoprazole 30 mg.

For excipients, see section 6.1

3 PHARMACEUTICAL FORM

Gastro-resistant capsule, hard.
Size 1 , white cap marked with 'L' and white body marked with '30', containing white to beige gastro-resistant micropellets.

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 H2 receptor antagonists.

4.2 Posology and method of administration

Dosage:
Gastro Oesophageal Reflux Disease: Lansoprazole 30 mg once daily for 4 weeks. The majority of patients will be healed after the first course. For those patients not fully healed at this time, a further 4 weeks treatment at the same dosage should be given.

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

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

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

Acid-related dyspepsia: Intermittent courses, as required, of Lansoprazole 15 mg or 30 mg once daily for 2-4 weeks depending on the severity and persistence of symptoms. Patients who do not respond after 4 weeks, or who relapse shortly afterwards, should be investigated.

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

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

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

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

Hypersecretory conditions: The initial 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 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 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

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.

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.

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

4.5 Interaction with other medicinal products and other forms of interaction

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

For lansoprazole no clinical data on exposed pregnancies are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonic/foetal development, parturition or postnatal development.

The use of lansoprazole during pregnancy is not recommended.

It is not known whether lansoprazole is excreted in human breast milk. Animal studies have shown excretion of lansoprazole in milk. A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with lansoprazole should be made taking into account the benefit of breast-feeding to the child and the benefit of lansoprazole therapy to the woman.

The use of lansoprazole during breast feeding should be avoided unless considered essential.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

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

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

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

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

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

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

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

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

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

Gynaecomastia and impotence have been reported rarely.

4.9 Overdose

There is no information on the effect of overdosage. However, lansoprazole has been given at doses up to 120mg/day without significant adverse effects. Symptomatic and supportive therapy should be given as appropriate.
Lansoprazole is not significantly eliminated by haemodialysis. If necessary, gastric emptying, administration of charcoal and symptomatic therapy are recommended.

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.

5.2 Pharmacokinetic properties

Absorption

Lansoprazole is rapidly inactivated by gastric acid. Therefore it is formulated as enteric-coated granules in gelatin capsules. Lansoprazole is rapidly absorbed from the duodenum; peak plasma concentrations are achieved within 1.5 – 2.0 hours. Intake of food slows the absorption rate and reduces its bioavailability (AUC) by approximately 25%.

Distribution

The bioavailability after a single lansoprazole 30 mg dose and after repeated daily administration is 80 – 90%. The bioavailability of lansoprazole may be reduced if antacids and sucralfate are co-administered. Plasma protein binding is approximately 95%. This has no significant effect on other protein bound active substances.

Metabolism

Lansoprazole is mainly metabolised in the liver.
Lansoprazole is mainly catalysed by the enzyme CYP 2C19. CYP 3A4 also contributes to the metabolism of lansoprazole. CYP 2C19 is subject to genetic polymorphism and approximately 2 – 65 of the general population are termed poor metabolisers (PMs) who are homozygote for a mutant CYP 2C19 allele. PMs lack a functional CYP 2C19 enzyme. In these PMs, exposure of lansoprazole is several-fold higher than in extensive metabolisers.

Three metabolites have been identified in the plasma: the sulfone, 5-hydroxy lansoprazole and the sulfide. These metabolites have a negligible effect on acid secretion.

Excretion

The elimination half-life of lansoprazole is 1.0 – 2.0 hours. Half life is not changed during repeated dosing of lansoprazole. A single dose of lansoprazole has an inhibitory effect on

gastric acid secretion, which lasts for more than 24 hours. Since lansoprazole is activated in the parietal cells, its plasma concentration is not related to gastric acid secretion.

Approximately, 15 – 50% of the metabolites are excreted in the urine and the remainder in the faeces. Three metabolites have been identified in the urine namely: 5-hydroxy sulfone, 5-hydroxy sulphide and 5-hydroxy lansoprazole.

In patients with cirrhosis, the AUC of lansoprazole is significantly increased and the elimination half life is prolonged; however, no signs of accumulation have been detected.

The bioavailability of lansoprazole is not significantly changed in patients with renal insufficiency.

In the elderly, elimination of lansoprazole is slightly delayed.

5.3 Preclinical safety data

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

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, toxicity to reproduction or genotoxicity.

In two rat carcinogenicity studies, lansoprazole produced dose-related gastric ECL cell hyperplasia and ECL cell carcinoids associated with hypergastrinaemia due to inhibition of acid secretion. Intestinal metaplasia was also observed, as were Leydig cell hyperplasia and benign Leydig cell tumours. After 18 months of treatment retinal atrophy was observed. This was not seen in monkeys, dogs or mice.

In mouse carcinogenicity studies dose-related gastric ECL cell hyperplasia developed as well as liver tumours and adenoma of rete testis.

The clinical relevance of these findings is unknown.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule content:

Sugar spheres (sucrose and maize starch)
Sodium starch glycolate Type A
Sodium lauril sulfate
Povidone K30
Potassium oleate
Oleic acid
Hypromellose
Methacrylic acid - ethyl acrylate copolymer 1:1
Triethyl citrate
Titanium dioxide (E171)
Talc

Body composition:

Titanium dioxide (E171)
Gelatin

Cap Composition:

Titanium dioxide (E171)
Gelatin (Limited Bone Gelatin)
Water

Printing Ink:

Shellac (Lacca)
Propylene glycol
Ammonium hydroxide
Potassium hydroxide
Black iron oxide (E172)

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
2 years.

6.4 Special precautions for storage
Do not store above 30ºC. Store in the original package. Keep the bottle tightly closed to protect from moisture.

6.5 Nature and contents of container
HDPE bottle, polypropylene cap with intergral silica gel desiccant.

Packs of 7, 14, 28 or 56 capsules (2 x 28 capsules)
Not all pack sizes are marketed.

6.6 Special precautions for disposal
No special instructions.

7 MARKETING AUTHORISATION HOLDER
Olinka (UK) Limited,
38/40 Chamberlayne Rd.,
London NW10 3JE,
United Kingdom.

8 MARKETING AUTHORISATION NUMBER(S)
PL 08608/0121, 0123, 0125, 0127

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
03/08/2007

10 DATE OF REVISION OF THE TEXT
03/08/2007

PATIENT INFORMATION LEAFLET

Lansoprazole 15 mg & 30 mg Gastro-Resistant Capsules

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:

The name of your medicine is:
LANSOPRAZOLE 15 MG GASTRO-RESISTANT CAPSULES
LANSOPRAZOLE 30 MG GASTRO-RESISTANT CAPSULES

- The active substance is lansoprazole. Each gastro-resistant hard capsule has a white cap marked with L and white body marked with 15 or 30, it contains white to beige gastro-resistant microgranules of 15 mg or 30 mg lansoprazole.

- The other ingredients are:
sugar spheres (sucrose and maize starch), sodium starch glycolate, sodium laurilsulfate, povidone, potassium oleate, oleic acid, hypromellose, methacrylic acid - ethyl acrylate copolymer 1:1, triethyl citrate, titanium dioxide (E171), talc and gelatin. The printing ink on the capsules contains the following additional ingredients: shellac (lacca), propylene glycol, ammonium hydroxide, potassium hydroxide, black iron oxide (E172).

Lansoprazole 15 mg Capsules are supplied in bottles of 7, 14, 28 or 56 capsules (2 x bottles of 28 capsules). *

Lansoprazole 30 mg Capsules are supplied in bottles of 7, 14, 28 or 56 capsules (2 x bottles of 28 capsules). *
(only the marketed pack sizes will be stated on the printed leaflets)*

Lansoprazole Capsules are manufactured by
Laboratorios Belmac SA,
Polígono Industrial Malpica,
calle C,
50016 Zaragoza,
Spain.

Marketing Authorisation Holder
Olinka (UK) Limited,
38/40 Chamberlayne Rd.,
London NW10 3JE,
United Kingdom.

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

Lansoprazole belongs to a group of medicines called proton pump inhibitors. Proton pump inhibitors, like lansoprazole, reduce the amount of acid that your stomach makes.

You have been given lansoprazole because you have a condition caused by stomach acid. Lansoprazole will treat your condition as it is very good at reducing the amount of acid your stomach makes. Lansoprazole is given to:
- heal ulcers in your stomach or duodenum (part of the intestine), including ulcers that are caused by other medicines called Non-Steroidal Anti-Inflammatory Drugs (shortened to NSAIDs).
- heal your oesophagus (gullet) if it has become damaged or inflamed. This is called Gastro-Oesophageal Reflux Disease.
- relieve you from the unpleasant symptoms that often occur with these conditions.
- stop these conditions coming back.

Lansoprazole is sometimes given to stop you getting an ulcer while you are taking an NSAID. Lansoprazole also takes away the pain of heartburn or indigestion and other unpleasant symptoms that can occur with the condition known as acid-related dyspepsia. Lansoprazole is sometimes given to patients whose stomach makes too much acid; this includes a condition called Zollinger-Ellison syndrome.

2. BEFORE YOU TAKE LANSOPRAZOLE CAPSULES

Do not take Lansoprazole Capsules:
- if you are hypersensitive (allergic) to lansoprazole or to any of the ingredients of the capsules. Check the ingredients listed near the beginning of this leaflet.

It is important to talk to your doctor if you have any of the following conditions:
- if you suffer from liver problems.
- if you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

Pregnancy and Breast-feeding:
Ask your doctor or pharmacist for advice before taking any medicine. Inform your doctor if you are pregnant, planning to become pregnant or if you are breast-feeding. Your doctor will decide if you should take Lansoprazole Capsules.

Driving and using machines:
There should be no effect on the ability to drive and operate machinery.

Taking other medicines:
Please inform your doctor or pharmacist if you are taking or have recently taken any other medicines, even those not prescribed. In particular, tell your doctor if you are taking any of the following medicines:
- the contraceptive pill.
- theophylline, which is sometimes used to treat asthma.
- phenytoin or carbamazepine, which are sometimes used to treat epilepsy.
- warfarin, which is a medicine sometimes used to thin the blood.
- other indigestion remedies.

Other precautions you should take:
If you are going to have an operation and anaesthetic (including at the dentist), tell your doctor or dentist that you are taking Lansoprazole Capsules.

3. HOW TO TAKE LANSOPRAZOLE CAPSULES

Swallow the capsule whole. If you find the capsules difficult to take, a drink of water at the same time might

make it easier. Do not crush or chew these capsules because this will stop them from working properly.

The dose of Lansoprazole Capsules depends on your condition and you should take your medicine exactly as your doctor has told you to.

- Your doctor will tell you how long your treatment with Lansoprazole Capsules will last. Do not stop treatment early, even if your symptoms have improved.
- Read the chemist's label to remind you how many capsules you should take and when you should take them.
- If you are taking Lansoprazole Capsules once a day, try to take it at the same time each day. You may get the best results if you take Lansoprazole Capsules first thing in the morning before breakfast.
- If you are taking Lansoprazole Capsules twice a day, you should take the first dose in the morning before breakfast and the second dose in the evening.

It is important to remember to take your medicine. If you do forget to take a dose, take it as soon as you remember unless it is nearly time for your next dose and continue as normal. Do not take a double dose. If you take more Lansoprazole Capsules than you have been told to, get medical advice quickly.

The usual doses of Lansoprazole Capsules for adults are given below. Sometimes your doctor will prescribe you a different dose.

If you have liver problems your doctor may limit your dose to one capsule a day.

HEALING OF STOMACH ULCERS
Take one 30 mg capsule every day for 8 weeks

PREVENTION OF AN ULCER AND RELIEF OF SYMPTOMS WHILE YOU TAKE AN NSAID
Take one 15 mg or 30 mg capsule every day for as long as your doctor prescribes.

GASTRO-OESOPHAGEAL REFLUX DISEASE
Take one 30 mg capsule a day for 4 to 8 weeks to heal your oesophagus and/or relieve symptoms. *Your doctor might prescribe a further* 15 mg or 30 mg capsule a day to prevent your condition coming back.

ACID-RELATED DYSPEPSIA
Take one 15 mg or 30 mg capsule every day for 2 to 4 weeks. *If your symptoms do not get better after this time, go back to your doctor.*

DUODENAL ULCERS
Take one 30 mg capsule every day for 4 weeks. *Your doctor might prescribe a further* 15 mg capsule every day to prevent your ulcer coming back.

STOMACH AND DUODENAL ULCERS CAUSED BY AN NSAID
Take one 15 mg or 30 mg capsule every day for 4 or 8 weeks. *Your doctor might prescribe a further* 15 mg or 30 mg capsule every day to prevent your ulcer or your symptoms coming back.

CONDITIONS WHERE YOUR STOMACH MAKES TOO MUCH ACID SUCH AS ZOLLINGER-ELLISON SYNDROME
Take two 30 mg capsules every day. Then, *depending on how you respond,* your doctor may change your dose.

There is no experience of this product in children.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Lansoprazole Capsules can have side effects. These are usually mild and go away when you stop taking this medicine.

If any of the following happens, stop taking the capsules and tell your doctor immediately or go to the casualty department at your nearest hospital:

- An allergic reaction (angioedema): e.g. swelling of the face, lips, tongue or throat, or difficulty breathing or swallowing.
- Colitis (persistent and severe diarrhoea leading to significant weight loss).
- Jaundice (yellowing of the skin or whites of the eyes).
- Severe reddening and blistering of the skin.
- Unexpected bruising or bleeding.

The side effects listed above, although serious and requiring medical attention, are extremely rare.

Common side effects:
The most common side effects are headache, dizziness, tiredness and generally feeling unwell.

Rare side effects:
There have been rare reports of joint and muscle pain, swollen limbs, blurred vision, larger breasts in women or breast development in men, impotence, blood disorders, taste disorders, kidney or liver problems, pins and needles and, numbness.

Skin reactions including skin blistering, urticaria (characterised by large red wheals in the skin) and pruritis (itching) can occur. Rarely, much more severe skin reactions occur; these affect large areas of the skin associated with redness, rash, blistering and peeling.

Other side-effects sometimes seen are stomach upsets including diarrhoea or constipation, feeling or being sick, wind and stomach ache.

Very rare side effects:
Very rarely, you may feel sleepy, confused, nervous, depressed or you may hallucinate.

Soreness of the mouth and throat, or a dry mouth, might occur.

Side effects also include sensitivity to light and hair loss.

The natural acid in your stomach helps to kill bacteria. Taking medicines like Lansoprazole Capsules, which reduce the amount of acid in the stomach, can lead to certain stomach infections.

You should see your doctor as soon as possible if you:

- get very bad or persistent diarrhoea.
- keep being sick (vomiting).
- notice any of the effects listed above.

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

5. STORING LANSOPRAZOLE CAPSULES

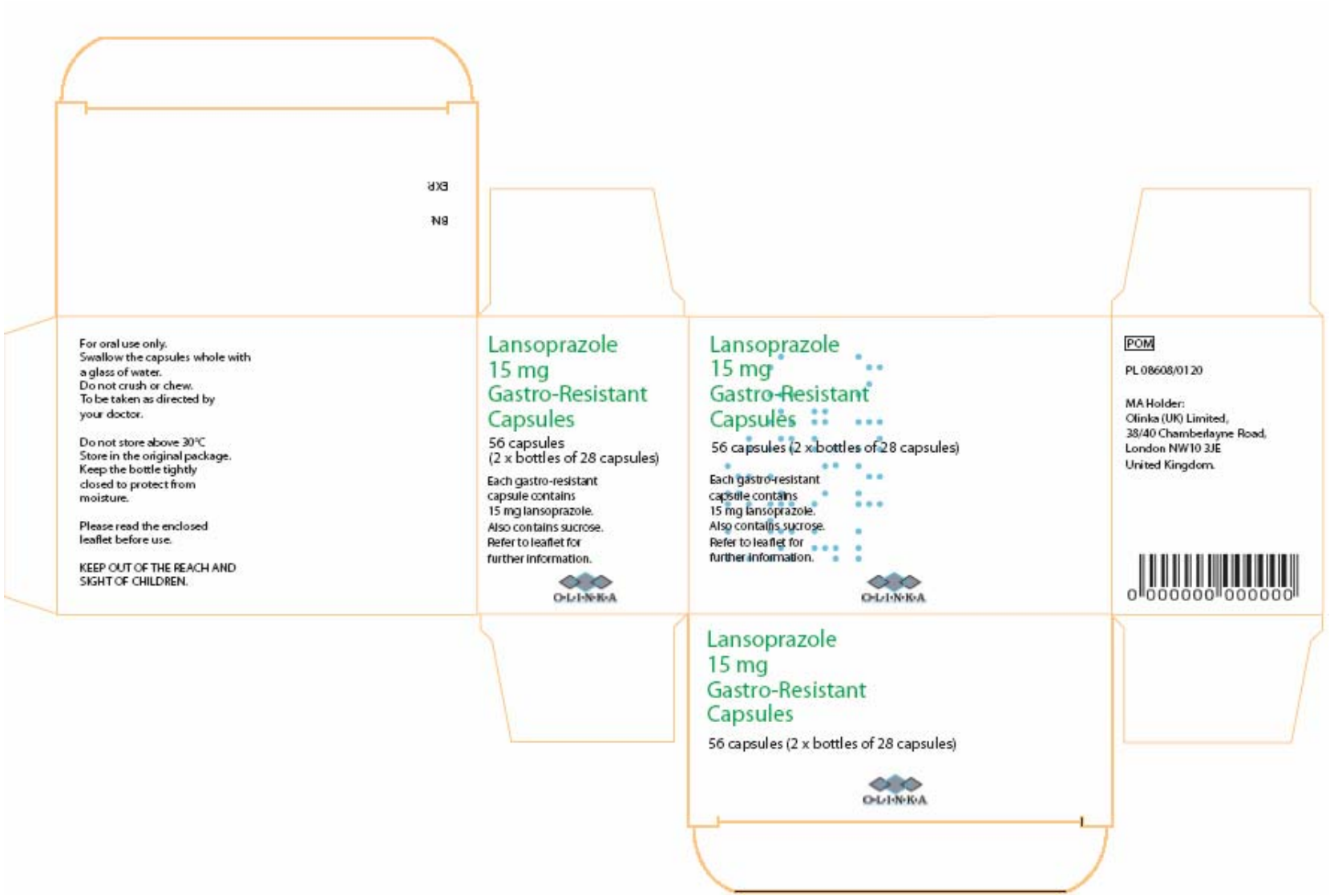
Do not store above 30°C. Store in the original package. Keep the bottle tightly closed to protect from moisture.

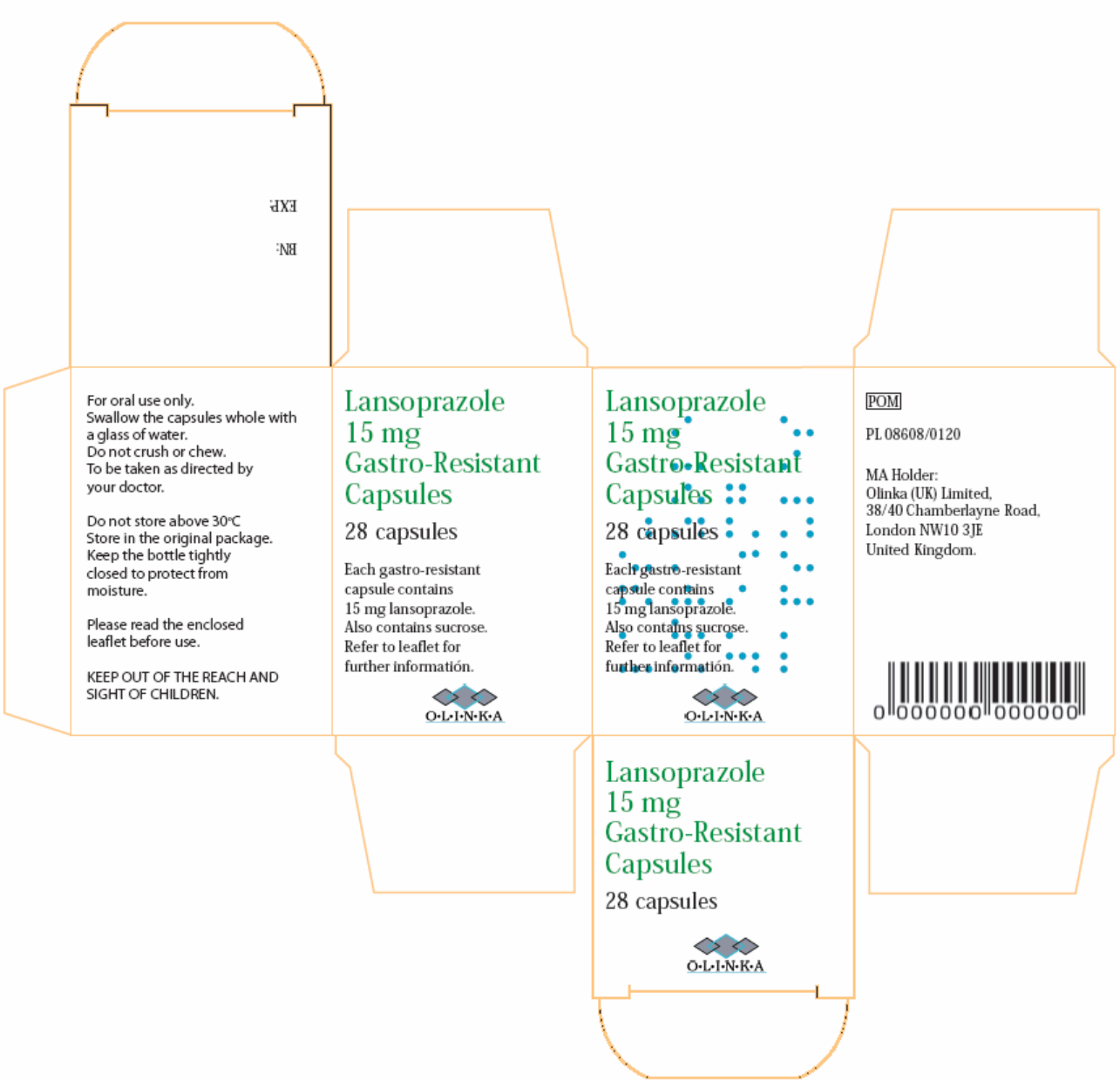
Keep out of the reach and sight of children.

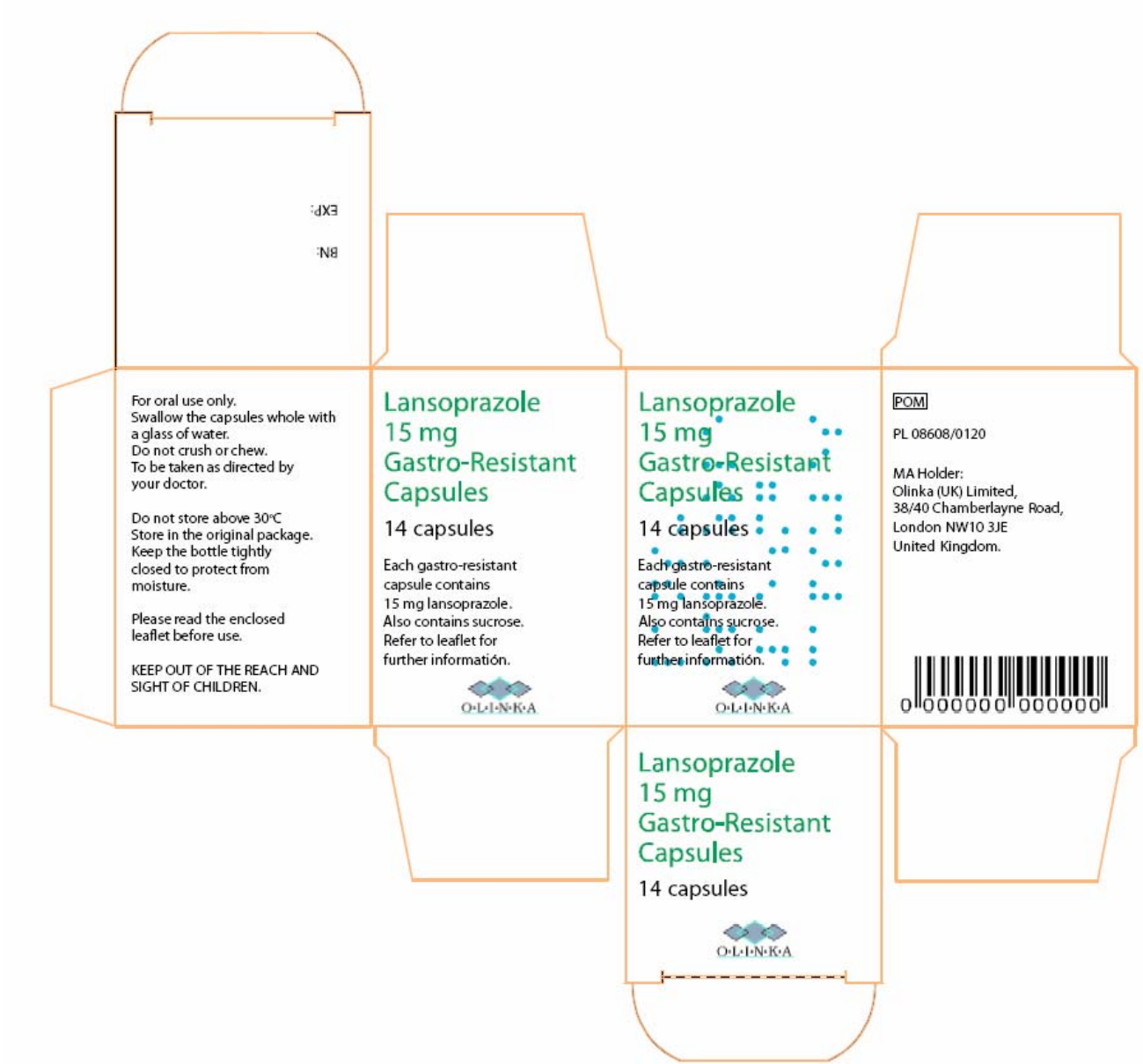
Do not use after the expiry date stated on the label.

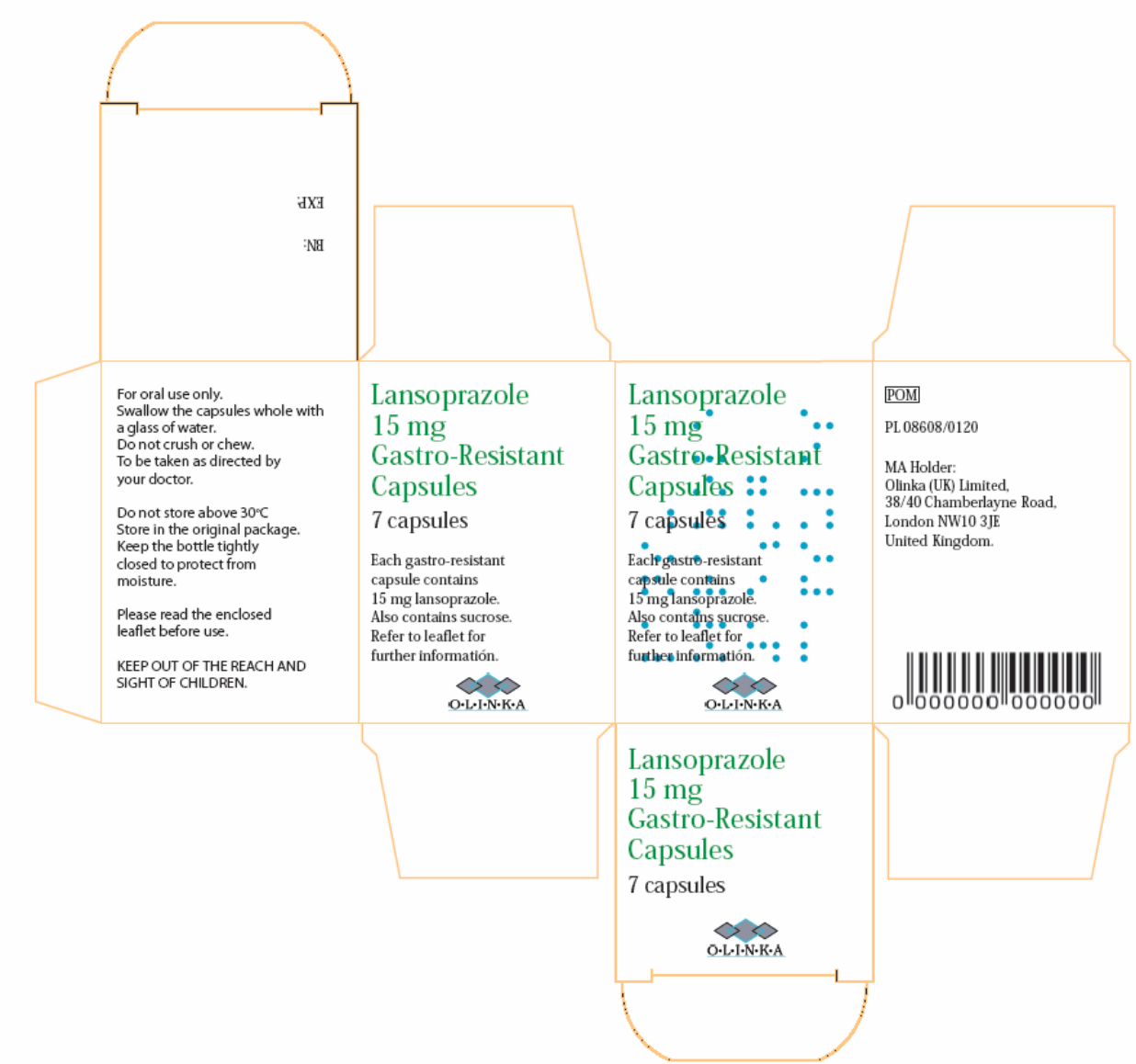
This leaflet was last updated in February 2006.

O·L·I·N·K·A


EXP
BN
For oral use only.
Swallow the capsules whole with a glass of water.
Do not crush or chew.
To be taken as directed by your doctor.
Do not store above 30°C
Store in the original package.
Keep the bottle tightly closed to protect from moisture.
Please read the enclosed leaflet before use.
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
Lansoprazole 15 mg Gastro-Resistant Capsules
56 capsules (2 x bottles of 28 capsules)
Each gastro-resistant capsule contains 15 mg lansoprazole.
Also contains sucrose.
Refer to leaflet for further information.
O·L·I·N·K·A
Lansoprazole 15 mg Gastro-Resistant Capsules
56 capsules (2 x bottles of 28 capsules)
Each gastro-resistant capsule contains 15 mg lansoprazole.
Also contains sucrose.
Refer to leaflet for further information.
O·L·I·N·K·A
POM
PL 08608/0120
MA Holder:
Olinka (UK) Limited,
38/40 Chamberlayne Road,
London NW10 3JE
United Kingdom.
0 000000 000000
Lansoprazole 15 mg Gastro-Resistant Capsules
56 capsules (2 x bottles of 28 capsules)
O·L·I·N·K·A


EXP:
For oral use only.
Swallow the capsules whole with a glass of water.
Do not crush or chew.
To be taken as directed by your doctor.
Do not store above 30°C
Store in the original package.
Keep the bottle tightly closed to protect from moisture.
Please read the enclosed leaflet before use.
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
Lansoprazole 15 mg Gastro-Resistant Capsules
28 capsules
Each gastro-resistant capsule contains 15 mg lansoprazole.
Also contains sucrose.
Refer to leaflet for further information.
O·L·I·N·K·A
Lansoprazole 15 mg Gastro-Resistant Capsules
28 capsules
Each gastro-resistant capsule contains 15 mg lansoprazole.
Also contains sucrose.
Refer to leaflet for further information.
O·L·I·N·K·A
POM
PL 08608/0120
MA Holder:
Olinka (UK) Limited,
38/40 Chamberlayne Road,
London NW10 3JE
United Kingdom.
Lansoprazole 15 mg Gastro-Resistant Capsules
28 capsules
O·L·I·N·K·A

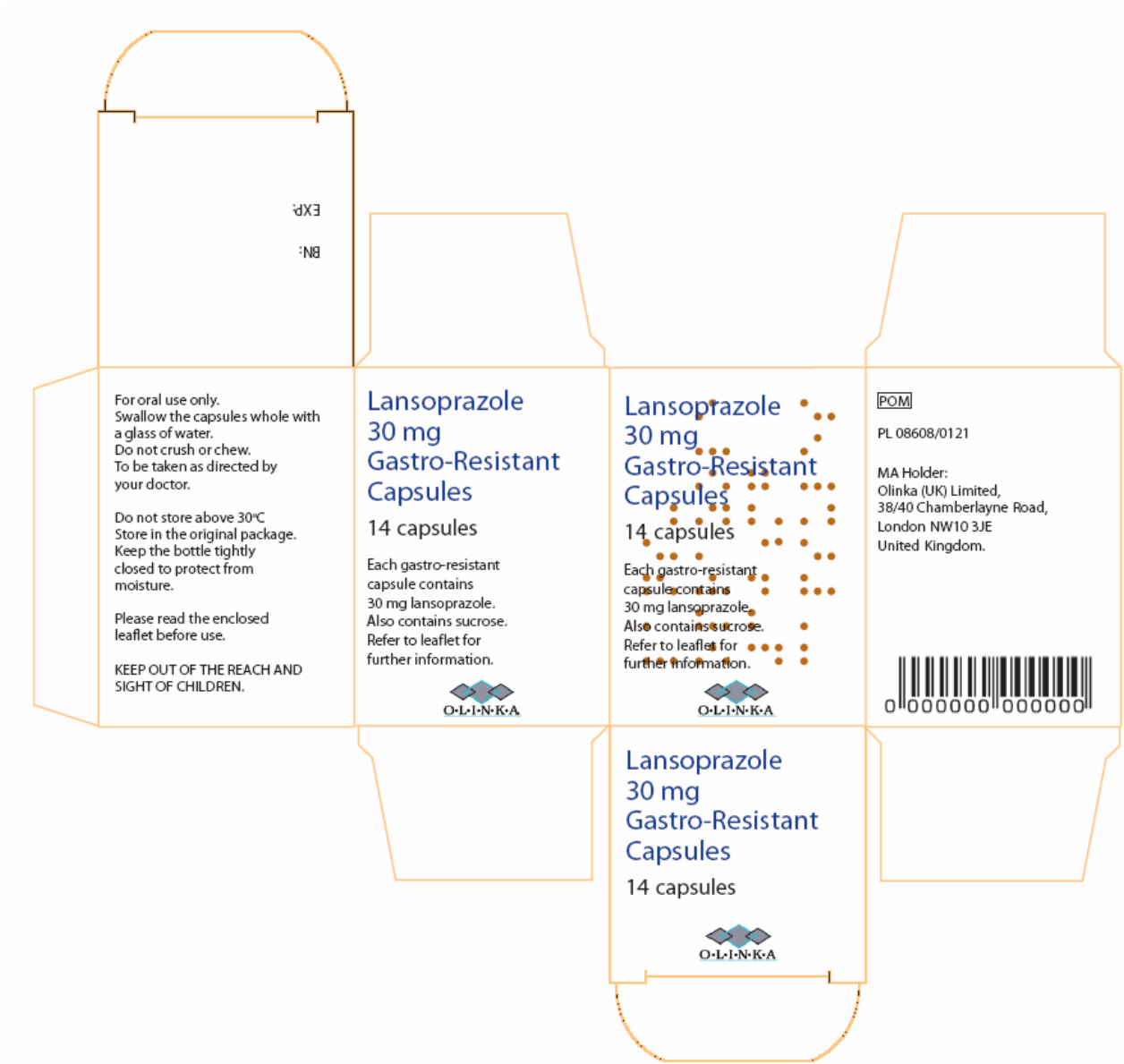

EXP:
BN:
For oral use only.
Swallow the capsules whole with a glass of water.
Do not crush or chew.
To be taken as directed by your doctor.
Do not store above 30°C
Store in the original package.
Keep the bottle tightly closed to protect from moisture.
Please read the enclosed leaflet before use.
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
Lansoprazole 15 mg Gastro-Resistant Capsules
14 capsules
Each gastro-resistant capsule contains 15 mg lansoprazole.
Also contains sucrose.
Refer to leaflet for further information.
O·L·I·N·K·A
Lansoprazole 15 mg Gastro-Resistant Capsules
14 capsules
Each gastro-resistant capsule contains 15 mg lansoprazole.
Also contains sucrose.
Refer to leaflet for further information.
O·L·I·N·K·A
POM
PL 08608/0120
MA Holder:
Olinka (UK) Limited,
38/40 Chamberlayne Road,
London NW10 3JE
United Kingdom.
Lansoprazole 15 mg Gastro-Resistant Capsules
14 capsules
O·L·I·N·K·A

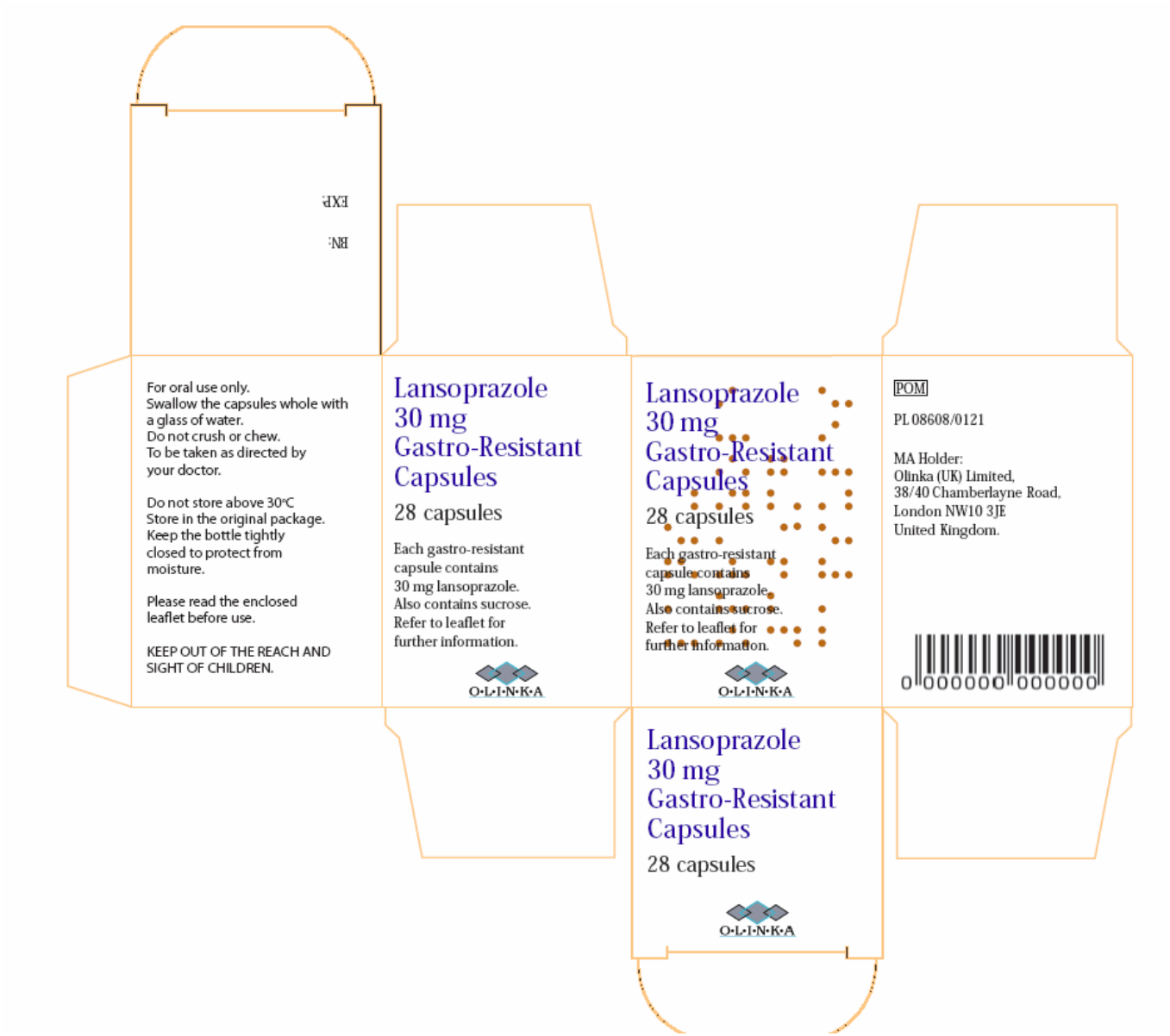

EXP:
BN:
For oral use only.
Swallow the capsules whole with a glass of water.
Do not crush or chew.
To be taken as directed by your doctor.
Do not store above 30°C
Store in the original package.
Keep the bottle tightly closed to protect from moisture.
Please read the enclosed leaflet before use.
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
Lansoprazole 15 mg Gastro-Resistant Capsules
7 capsules
Each gastro-resistant capsule contains 15 mg lansoprazole.
Also contains sucrose.
Refer to leaflet for further information.
O·L·I·N·K·A
Lansoprazole 15 mg Gastro-Resistant Capsules
7 capsules
Each gastro-resistant capsule contains 15 mg lansoprazole.
Also contains sucrose.
Refer to leaflet for further information.
O·L·I·N·K·A
POM
PL 08608/0120
MA Holder:
Olinka (UK) Limited,
38/40 Chamberlayne Road,
London NW10 3JE
United Kingdom.
0 000000 000000
Lansoprazole 15 mg Gastro-Resistant Capsules
7 capsules
O·L·I·N·K·A

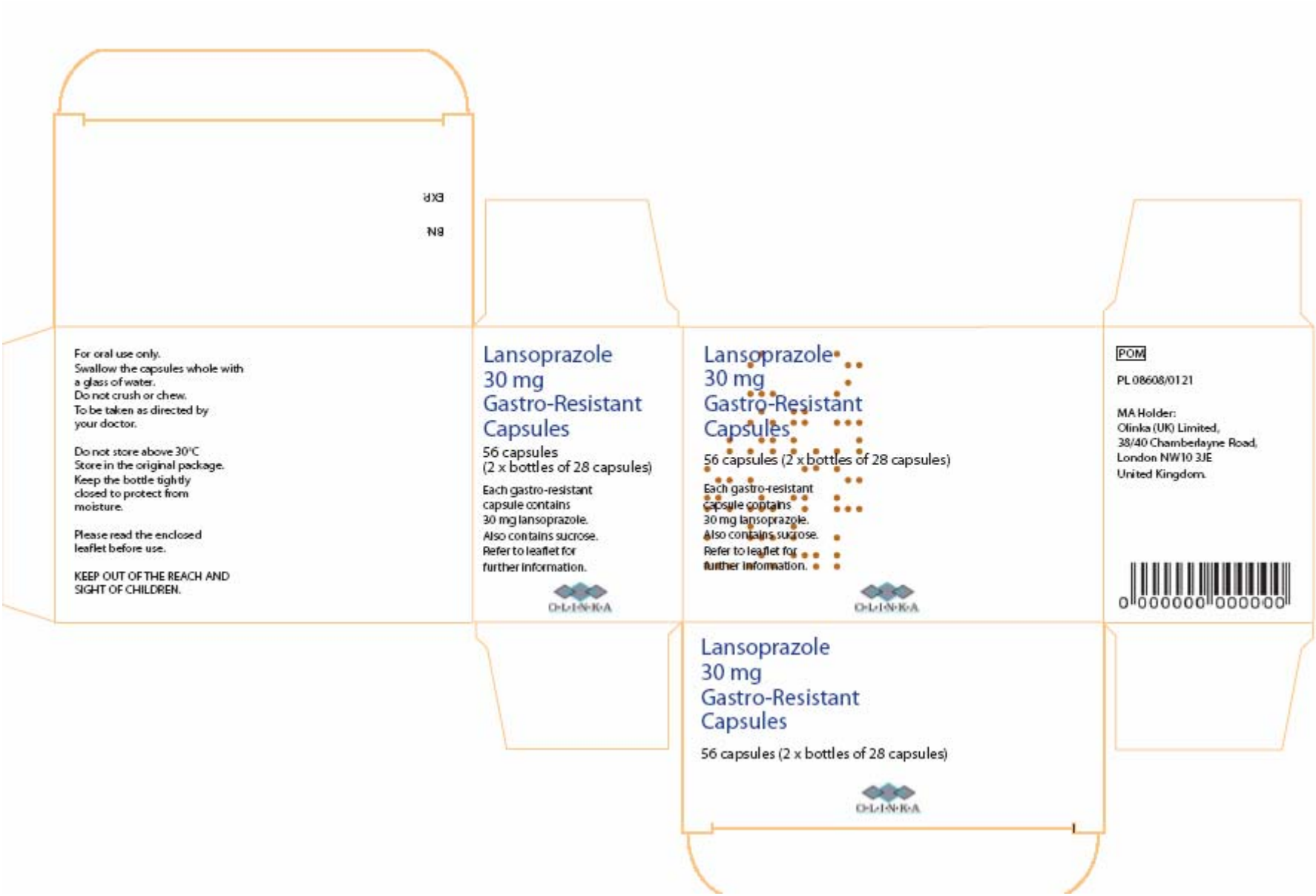
Lansoprazole 15 mg Gastro-Resistant Capsules KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
28 capsules. Each capsule contains 15 mg lansoprazole. Also contains sucrose - see leaflet. For oral use only. Take as directed by your doctor.
Do not store above 30°C. Store in the original package. Keep the bottle tightly closed to protect from moisture. BN: EXP:
MA Holder: Olinka (UK) Limited, 38/40 Chamberlayne Road, London NW10 3JE. PL 08608/0120 POM

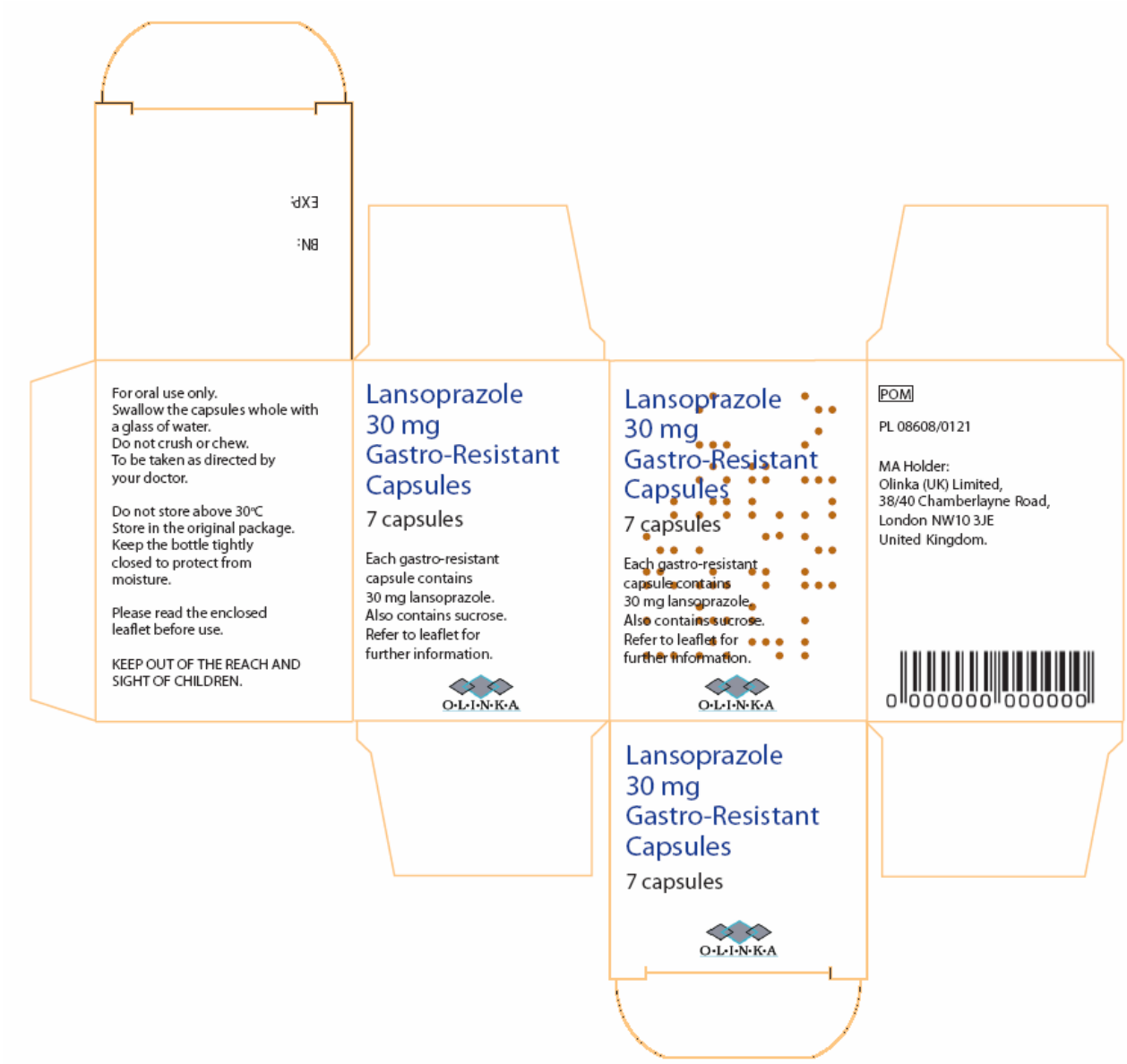
Lansoprazole 15 mg Gastro-Resistant Capsules KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
14 capsules. Each capsule contains 15 mg lansoprazole. Also contains sucrose - see leaflet. For oral use only. Take as directed by your doctor.
Do not store above 30°C. Store in the original package. Keep the bottle tightly closed to protect from moisture. BN: EXP:
MA Holder: Olinka (UK) Limited, 38/40 Chamberlayne Road, London NW10 3JE. PL 08608/0120 POM

Lansoprazole 15 mg Gastro-Resistant Capsules KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
7 capsules. Each capsule contains 15 mg lansoprazole. Also contains sucrose - see leaflet. For oral use only. Take as directed by your doctor.
Do not store above 30°C. Store in the original package. Keep the bottle tightly closed to protect from moisture. BN: EXP:
MA Holder: Olinka (UK) Limited, 38/40 Chamberlayne Road, London NW10 3JE. PL 08608/0120 POM


EXP:
BN:
For oral use only.
Swallow the capsules whole with a glass of water.
Do not crush or chew.
To be taken as directed by your doctor.
Do not store above 30°C
Store in the original package.
Keep the bottle tightly closed to protect from moisture.
Please read the enclosed leaflet before use.
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
Lansoprazole 30 mg Gastro-Resistant Capsules
14 capsules
Each gastro-resistant capsule contains 30 mg lansoprazole.
Also contains sucrose.
Refer to leaflet for further information.
O·L·I·N·K·A
Lansoprazole 30 mg Gastro-Resistant Capsules
14 capsules
Each gastro-resistant capsule contains 30 mg lansoprazole.
Also contains sucrose.
Refer to leaflet for further information.
O·L·I·N·K·A
POM
PL 08608/0121
MA Holder:
Olinka (UK) Limited,
38/40 Chamberlayne Road,
London NW10 3JE
United Kingdom.
0 000000 000000
Lansoprazole 30 mg Gastro-Resistant Capsules
14 capsules
O·L·I·N·K·A


EXP:
BN:
For oral use only.
Swallow the capsules whole with a glass of water.
Do not crush or chew.
To be taken as directed by your doctor.
Do not store above 30ºC
Store in the original package.
Keep the bottle tightly closed to protect from moisture.
Please read the enclosed leaflet before use.
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
Lansoprazole 30 mg Gastro-Resistant Capsules
28 capsules
Each gastro-resistant capsule contains 30 mg lansoprazole.
Also contains sucrose.
Refer to leaflet for further information.
O·L·I·N·K·A
Lansoprazole 30 mg Gastro-Resistant Capsules
28 capsules
Each gastro-resistant capsule contains 30 mg lansoprazole.
Also contains sucrose.
Refer to leaflet for further information.
O·L·I·N·K·A
POM
PL 08608/0121
MA Holder:
Olinka (UK) Limited,
38/40 Chamberlayne Road,
London NW10 3JE
United Kingdom.
0 000000 000000
Lansoprazole 30 mg Gastro-Resistant Capsules
28 capsules
O·L·I·N·K·A


EXP
BN
For oral use only.
Swallow the capsules whole with a glass of water.
Do not crush or chew.
To be taken as directed by your doctor.
Do not store above 30°C
Store in the original package.
Keep the bottle tightly closed to protect from moisture.
Please read the enclosed leaflet before use.
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
Lansoprazole 30 mg Gastro-Resistant Capsules
56 capsules (2 x bottles of 28 capsules)
Each gastro-resistant capsule contains 30 mg lansoprazole.
Also contains sucrose.
Refer to leaflet for further information.
O·L·I·N·K·A
Lansoprazole 30 mg Gastro-Resistant Capsules
56 capsules (2 x bottles of 28 capsules)
Each gastro-resistant capsule contains 30 mg lansoprazole.
Also contains sucrose.
Refer to leaflet for further information.
O·L·I·N·K·A
POM
PL 08608/0121
MA Holder:
Olinka (UK) Limited,
38/40 Chamberlayne Road,
London NW10 3JE
United Kingdom.
0 000000 000000
Lansoprazole 30 mg Gastro-Resistant Capsules
56 capsules (2 x bottles of 28 capsules)
O·L·I·N·K·A


EXP:
BN:
For oral use only.
Swallow the capsules whole with a glass of water.
Do not crush or chew.
To be taken as directed by your doctor.
Do not store above 30°C
Store in the original package.
Keep the bottle tightly closed to protect from moisture.
Please read the enclosed leaflet before use.
KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
Lansoprazole 30 mg Gastro-Resistant Capsules
7 capsules
Each gastro-resistant capsule contains 30 mg lansoprazole.
Also contains sucrose.
Refer to leaflet for further information.
O·L·I·N·K·A
Lansoprazole 30 mg Gastro-Resistant Capsules
7 capsules
Each gastro-resistant capsule contains 30 mg lansoprazole.
Also contains sucrose.
Refer to leaflet for further information.
O·L·I·N·K·A
POM
PL 08608/0121
MA Holder:
Olinka (UK) Limited,
38/40 Chamberlayne Road,
London NW10 3JE
United Kingdom.
0 000000 000000
Lansoprazole 30 mg Gastro-Resistant Capsules
7 capsules
O·L·I·N·K·A

Lansoprazole 30 mg Gastro-Resistant Capsules KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
14 capsules. Each capsule contains 30 mg lansoprazole. Also contains sucrose - see leaflet. For oral use only. Take as directed by your doctor.
Do not store above 30ºC. Store in the original package. Keep the bottle tightly closed to protect from moisture. BN: EXP:
MA Holder: Olinka (UK) Limited, 38/40 Chamberlayne Road, London NW10 3JE. PL 08608/0121 POM

Lansoprazole 30 mg Gastro-Resistant Capsules KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
28 capsules. Each capsule contains 30 mg lansoprazole. Also contains sucrose - see leaflet.
Do not store above 30ºC. Store in the original package. Keep the bottle tightly closed to protect from moisture.
For oral use only. Take as directed by your doctor. PL 08608/0121 POM BN: EXP:
MA Holder: Olinka (UK) Limited, 38/40 Chamberlayne Road, London NW10 3JE.

Lansoprazole 30 mg Gastro-Resistant Capsules KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.
7 capsules. Each capsule contains 30 mg lansoprazole. Also contains sucrose - see leaflet. For oral use only. Take as directed by your doctor.
Do not store above 30ºC. Store in the original package. Keep the bottle tightly closed to protect from moisture. BN: EXP:
MA Holder: Olinka (UK) Limited, 38/40 Chamberlayne Road, London NW10 3JE. PL 08608/0121 POM