

**LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES  
PL 21561/0001**

**LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES  
PL 21561/0002**

**UKPAR**

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**LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES  
PL 21561/0001**

**LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES  
PL 21561/0002**

**LAY SUMMARY**

The MHRA today granted Dexter Farmaceutica Marketing Authorisations (licences) for the medicinal products Lansoprazole 15mg Capsules (PL 21561/0001) and Lansoprazole 30mg Capsules (PL 21561/0002). 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 Capsules contain the active ingredient lansoprazole, which acts by reducing gastric acidity, a key requirement for healing of acid-related disorders such as peptic ulcers.

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

**LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES  
PL 21561/0001**

**LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES  
PL 21561/0002**

**SCIENTIFIC DISCUSSION**

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## **INTRODUCTION**

Based on the review of the data on quality, safety and efficacy the UK granted marketing authorisations for the medicinal products Lansoprazole 15mg and 30mg Gastro-resistant Capsules to Dexter Farmaceutica (PL 21561/0001-2) on 6<sup>th</sup> December 2005. The products are prescription only medicines.

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

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

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

## PHARMACEUTICAL ASSESSMENT

### **Active substance**

|                    |  |
|--------------------|--|
| INN:               | Lansoprazole   |
| Chemical Name:     | 2-[[[3-methyl-4-(2, 2, 2-trifluoroethoxy)- pyridine-2-yl]methyl]sulfinyl benzimidazole |
| Molecular Formula: | $C_{16}H_{14}F_3N_3O_2.S$  |
| Molecular Weight:  | 369.37   |
| Appearance:        | White or beige solid   |

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

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.

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

All potential known impurities have been identified and characterised.

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

Appropriate stability data have been generated and no indication of instability seen. The data support a retest period of 12 months when stored at 2-8°C in double PE bags placed in a metal drum with a metal clamp closure.

### **Other ingredients**

Other ingredients consist of hypromellose, talc, titanium dioxide, methacrylic acid-ethyl acrylate, triethyl citrate, sugar spheres, purified water and hard gelatin capsule (which itself consists of titanium dioxide E171, purified water, gelatin, and black printing ink). All excipients used in the capsule fill are routinely tested for compliance with their respective Ph Eur monograph. Hard gelatin capsules used comply with in-house specifications. The qualitative and quantitative composition of the printing ink is given and all ingredients comply with USP-NF requirements (iron oxide also meet EC quality requirements).

Satisfactory certificates of analysis have been provided for all ingredients.

Gelatin used in the manufacture of the capsules is the only material of animal or human origin used. Satisfactory certificates of suitability have been provided.

Both strength capsules are packaged in white HDPE bottles with tamper evident, screw cap closures containing silica gel as desiccant and a white tamper evident ring. Alternatively, the capsules are packaged in aluminium/aluminium blisters. Satisfactory specifications and certificates of analysis have been provided for the packaging components.

### **Product development and finished product**

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

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

Comparative *in vitro* dissolution profiles have been generated for the proposed and reference products with satisfactory results. Comparative impurity studies have also been undertaken.

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 at pilot-scale. Additionally, a commitment has been provided that the first full-scale commercial production batches will be validated.

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

### **Stability of the product**

All results from stability studies on pilot batches were within specified limits. These data support a shelf-life of 18 months for the 15 mg strength product packaged in the blister packs and 24 months for the 30 mg strength product packaged in the blister packs. They also support a shelf-life of 24 months (unopened) and 28 days (after opening) for either strength of product packaged in HDPE bottles with screw cap. Storage conditions are 'Do not store above 25°C. Store in the original package' for the blister packs and 'Do not store above 25°C. Keep the bottle tightly closed to protect from moisture' for the HDPE bottles.

### **Bioequivalence/bioavailability**

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

### **SPC, PIL, Labels**

The SPC, PIL and Labels are pharmaceutically acceptable.

**CONCLUSION**

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

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

## **PRECLINICAL ASSESSMENT**

These applications for generic products claims essential similarity to Lanzor 15 and 30mg Capsules (Aventis, France), which have been licensed within the EEA for over 10 years.

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

## CLINICAL ASSESSMENT

### 1. INTRODUCTION

These applications are submitted under Article 10.1(a)(iii) of the Directive 2001/83/EC. The applicant claims essential similarity to Lanzor 30mg capsules marketed in France by Aventis. The first Marketing Authorisation for lansoprazole hard capsules 30mg was in France in 1990 and subsequently in Germany in June 1993. In the UK it is marketed by Cyanamid of Great Britain (PLs 00095/0302 and 0264), granted in the UK 23<sup>rd</sup> February 1994 and 17 January 1996, respectively.

### 2. 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*.

### 3. 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<sub>2</sub> receptor antagonists.

#### Assessor's Comment

*These are consistent with those of the reference product license.*

### 4. DOSE & DOSE SCHEDULE

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

## 5. TOXICOLOGY

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

## 6. CLINICAL PHARMACOLOGY

### 6.1 Pharmacodynamics

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

### 6.2 Pharmacokinetics

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

### 6.3 Bioequivalence

The applicant has submitted a two-part study to determine the bioequivalence between the applicant's Lansoprazole 30mg capsules and the reference product following a single and multiple oral dose administration under fasting conditions and after a multiple oral dose administration under fed conditions. Both single and multiple doses parts of the study were performed in 52 healthy male and female volunteers.

In each study period, the drug was administered once daily on seven consecutive days under fasting conditions: an eighth dose was administered on the eighth day morning, thirty minutes after the beginning of a high fat breakfast. Each period was separated by a washout of 14 days. Blood samples were obtained at frequent intervals up to 12 hours and 24 hours post dosing following single and multiple dosing respectively. Lansoprazole was analysed using HPLC.

Statistical analysis was performed using Parametric ANOVA on  $C_{max}$ ,  $T_{max}$ ,  $AUC_T$  (or  $AUC_t$ ),  $AUC_{\infty}$ ,  $AUC_{T/\infty}$ , (or  $AUC_{t/\infty}$ ),  $K_{el}$  and  $T_{1/2el}$ ; geometric confidence interval for  $C_{max}$ ,  $AUC_T$  (or  $AUC_t$  and  $AUC_{\infty}$  based on In-transformed data;  $T_{max}$  rank transformed. Anova model was applied with regards to the following:

- Stratified by each of the three days (day 1, day 7, day 8)
- Fixed factors: treatment, period, sequence;
- Random factor: subject effect (nested within the sequence)

The criteria for bioequivalence were as follows:

- The 90% confidence interval for the exponential of the difference between the Test and the Reference product for the ln-transformed parameter  $AUC_T$  and  $AUC_\infty$  should be between 80 and 125%
- The 90% confidence interval for the exponential of the difference between the Test and the Reference product for the ln-transformed parameter  $C_{max}$  should be between 75 and 133.33%.

The results of the main pharmacokinetic parameters are summarised in the three tables presented below.

### Lansoprazole 30mg Capsule (N=52)

#### Single dose: Fasting (Day 1)

| Parameter                  | Geometric LS Means |           | Ratio | 90% Confidence Limits |        |
|----------------------------|--------------------|-----------|-------|-----------------------|--------|
|                            | TEST               | REFERENCE |       | LOWER                 | UPPER  |
| C <sub>max</sub> (ng/ml)   | 905.9              | 927.2     | 97.71 | 88.69                 | 107.63 |
| T <sub>max</sub> (hrs)     | 1.50               | 1.50      |       |                       |        |
| AUC <sub>t</sub> (ng.h/ml) | 1914.4             | 2070.7    | 92.45 | 86.78                 | 98.49  |
| AUC <sub>∞</sub> (ng.h/ml) | 1987.2             | 2164.3    | 91.81 | 86.30                 | 97.68  |

### Lansoprazole 30mg Capsule (N=52)

#### Following Multiple dosing: Fasting (Day 7)

| Parameter                  | Geometric LS Means |           | Ratio  | 90% Confidence Limits |        |
|----------------------------|--------------------|-----------|--------|-----------------------|--------|
|                            | TEST               | REFERENCE |        | LOWER                 | UPPER  |
| C <sub>max</sub> (ng/ml)   | 958.6              | 843.1     | 113.70 | 103.76                | 124.61 |
| T <sub>max</sub> (hrs)     | 1.50               | 1.75      |        |                       |        |
| AUC <sub>t</sub> (ng.h/ml) | 2090.7             | 2033.7    | 102.80 | 97.02                 | 108.92 |
| AUC <sub>∞</sub> (ng.h/ml) | 2200.0             | 2165.0    | 101.62 | 96.84                 | 106.62 |

### Lansoprazole 30mg Capsule (N=52)

#### Following Multiple dosing: Fed (Day 8)

| Parameter                  | Geometric LS Means |           | Ratio  | 90% Confidence Limits |        |
|----------------------------|--------------------|-----------|--------|-----------------------|--------|
|                            | TEST               | REFERENCE |        | LOWER                 | UPPER  |
| C <sub>max</sub> (ng/ml)   | 215.4              | 148.7     | 144.92 | 112.34                | 186.96 |
| T <sub>max</sub> (hrs)     | 4.50               | 3.33      |        |                       |        |
| AUC <sub>t</sub> (ng.h/ml) | 757.4              | 479.8     | 157.87 | 124.80                | 199.71 |
| AUC <sub>∞</sub> (ng.h/ml) | 1172.9             | 729.4     | 160.80 | 128.61                | 201.05 |

The Test formulation (Lansoprazole 30mg capsules) was shown to be bioequivalent to the Reference formulation only under fasting conditions following a single and multiple oral dose administration.

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

Forty-eight (48) subjects experienced a total of one-hundred-fifty-one (151) adverse events during the study. Seventy-three adverse events (35 different types) were reported after the single dose administration of the Test product and seventy-eight adverse events (37 different types) were reported after the administration of the Reference product. No serious adverse events were reported.

#### **Assessor's Comment**

*The results of the fasted study indicate unequivocal equivalence. The 90% confidence intervals (CI) for the AUC and  $C_{max}$  ratios fall within the conventional 80-125% bioequivalence range in the fasting study, but outside this range in the fed one.*

*The outside conventional bioequivalence range of CI shown in the fed study can be accepted in the case of lansoprazole particularly with its high intra-subject variability; for this implies a large range of blood drug levels, even when the same product is administered to the same subject on different occasions.*

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

#### **7. EFFICACY**

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

#### **8. SAFETY**

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

#### **9. EXPERT REPORT**

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

#### **10. SUMMARY OF PRODUCT CHARACTERISTICS**

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

#### **11. PATIENT INFORMATION LEAFLET**

This is satisfactory.

#### **12. LABELLING**

These appear satisfactory.

**13. DISCUSSION**

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

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

**14. CONCLUSION**

Overall, there are no clinical objections to the grant of a marketing authorisation 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 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 Lanzor 30mg capsules (Aventis, France). 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 Lanzor capsules

### 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 21561/0001**

**LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES  
PL 21561/0002**

**STEPS TAKEN FOR ASSESSMENT**

|   |  |
|---|--|
| 1 | The MHRA received the marketing authorisation applications on 14 <sup>th</sup> June 2004   |
| 2 | Following standard checks and communication with the applicant the MHRA considered the applications valid on 28 <sup>th</sup> June 2004  |
| 3 | Following assessment of the applications the MHRA requested further information relating to the clinical dossiers on 3 <sup>rd</sup> December 2004, and further information relating to the quality dossiers on 8 <sup>th</sup> June 2005. |
| 4 | The applicant responded to the MHRA's requests, providing further information on 29 <sup>th</sup> June 2005, and again on 28 <sup>th</sup> July 2005.  |
| 7 | The applications were determined on 6 <sup>th</sup> December 2005  |

**LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES  
PL 21561/0001**

**LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES  
PL 21561/0002**

**STEPS TAKEN AFTER AUTHORISATION - SUMMARY**

| <b>Date submitted</b> | <b>Application type</b> | <b>Scope</b> | <b>Outcome</b> |
|-----------------------|-------------------------|--------------|----------------|
|                       |                         |              |                |
|                       |                         |              |                |
|                       |                         |              |                |
|                       |                         |              |                |
|                       |                         |              |                |

**1. NAME OF THE MEDICINAL PRODUCT**

Lansoprazole 15 mg gastro-resistant capsules

**2. QUALITATIVE AND QUANTITATIVE COMPOSITION**

Each gastro-resistant capsule contains 15 mg of lansoprazole.

For excipients, see 6.1.

**3. PHARMACEUTICAL FORM**

Gastro-resistant capsules, hard

Size 3, opaque white hard gelatin capsule printed LAN 15, containing white to slightly pink/beige spherical pellets

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

Healing of benign gastric ulcer.

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

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

Lansoprazole is also effective in patients with benign peptic lesions, including reflux oesophagitis, unresponsive to H<sub>2</sub> receptor antagonists.

**4.2. Posology and method of administration****Dosage:**

Gastro Oesophageal Reflux Disease: Lansoprazole 30 mg gastro-resistant capsules 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 gastro-resistant capsules once daily can be used dependent upon patient response.

Duodenal ulcer: Lansoprazole 30 mg gastro-resistant capsules once daily for 4 weeks.

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

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

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

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

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

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

For patients who require 120mg 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 before a meal. 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 capsules 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 30mg are administered to patients with severe hepatic impairment. It is therefore

recommended that the daily dose for patients with severe liver disease is individually adjusted to 15mg or 30mg. These patients should be kept under regular supervision and a daily dosage of 30mg should not be exceeded.

There is no need to alter the dosage in patients with mild to moderate impairment of hepatic function or impaired renal function.

#### **4.3 Contraindications**

The use of lansoprazole is contra-indicated in patients with a history of hypersensitivity to any of the ingredients of Lansoprazole 15mg or 30 mg gastro-resistant 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 medicine contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

#### **4.5 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 15mg or 30 mg gastro-resistant capsules.

#### **4.6 Pregnancy and lactation**

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

The use of lansoprazole in pregnancy should be avoided.

Animal studies indicate that lansoprazole is secreted in breast milk.

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

#### **4.7 Effects on ability to drive and use machines**

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

#### **4.8 Undesirable effects**

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

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

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

As with other PPIs, very rarely, cases of colitis have been reported.

In severe and/or protracted cases of diarrhoea, discontinuation of therapy should be considered. In the majority of cases symptoms resolve on discontinuation of therapy.

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

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

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

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

Other reactions include arthralgia, myalgia, depression, peripheral oedema and,

rarely, paraesthesia, blurred vision, taste disturbances, vertigo, confusion and hallucinations.

Gynaecomastia and impotence have been reported rarely.

#### 4.9 Overdose

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

### 5. PHARMACOLOGICAL PROPERTIES

#### 5.1. Pharmacodynamic properties

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 sulphhydryl group of the  $H^+ / K^+$  ATPase causing inhibition. This inhibition is reversible *in vitro* by intrinsic and extrinsic reducing agents. Lansoprazole's mode of action differs significantly from the  $H_2$  antagonists which inhibit one of the three pathways involved in stimulation of acid production. A single dose of 30mg inhibits pentagastrin-stimulated acid secretion by approximately 80%, indicating effective acid inhibition from the first day of dosing.

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

By reducing gastric acidity, Lansoprazole 15, 30 mg capsules creates an environment in which appropriate antibiotics can be effective against *H. pylori*. *In vitro* studies have shown that lansoprazole has a direct antimicrobial effect on *H. pylori*.

#### 5.2. Pharmacokinetic properties

Lansoprazole exhibits high (80-90%) bioavailability with a single dose. As a result, effective acid inhibition is achieved rapidly. Peak plasma levels occurred within 1.5 to 2.0 hours. The plasma elimination half-life ranges from 1 to 2 hours following single or multiple doses in healthy subjects. There is no evidence of accumulation following multiple doses in healthy subjects. The plasma protein binding is 97%.

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

#### 5.3. Preclinical safety data

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

An increased incidence of spontaneous retinal atrophy has been observed in life-long studies in rats. These lesions which are common to albino laboratory rats have not been observed in monkeys or dogs or life-long studies in mice. They are considered to

be rat specific. No such treatment related changes have been observed in patients treated continuously for long periods.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipient(s)

**Capsules contents:** Hypromellose (E-464), Talc (E-553b), Titanium dioxide (E-171), Metacrylic acid-ethyl acrylate copolymer (1:1) dispersion 30% , Triethylcitrate (E-1505), Sugar spheres (sucrose and maize starch)

**Capsule Shells:** Titanium dioxide (E-171), Purified water, Gelatine.

**Printing ink:** shellac and black iron oxide (E-172).

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf-life

HDPE: 24 months. In-use stability has been demonstrated for 28 days

Blister (Al/Al): 18 months

### 6.4 Special precautions for storage

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

Bottle pack: Do not store above 25°C. Keep the bottle tightly closed to protect from moisture.

### 6.5 Nature and contents of container

Bottle packs: HDPE container and screw cap with tamper evident ring containing a desiccant capsule (LDPE)

Bottles of 7, 14, 28 and 56 (28x2) capsules

Blister packs: Al/Al foil. Each blister strip contains 7 capsules.

Blister packs of 7 (1 blister strip), 14 (2 blister strips), 28 (4 blister strips), 42 (6 blister strips) and 56 (8 blister strips) capsules

Not all pack sizes may be marketed

### 6.6 Instructions for use and handling

No special requirements.

## 7. MARKETING AUTHORISATION HOLDER

Dexter Farmacéutica, S.A.

Avda. Mare de Déu de Montserrat, 215

08041 Barcelona

Spain

## 8. MARKETING AUTHORISATION NUMBER

PL 21561/0001

**9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE  
AUTHORISATION**

06/12/2005

**10 DATE OF REVISION OF THE TEXT**

06/12/2005

## SUMMARY OF PRODUCT CHARACTERISTICS

### 1. NAME OF THE MEDICINAL PRODUCT

Lansoprazole 30 mg gastro-resistant capsules

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gastro-resistant capsule contains 30 mg of lansoprazole

For excipients see 6.1.

### 3. PHARMACEUTICAL FORM

Gastro-resistant capsules, hard

Size 1 opaque white hard gelatine capsule printed LAN 30, containing white to slightly pink/beige spherical pellets

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

Healing of benign gastric ulcer.

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

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

Lansoprazole is also effective in patients with benign peptic lesions, including reflux oesophagitis, unresponsive to H<sub>2</sub> receptor antagonists.

### 4.2 Posology and method of administration

#### **Dosage:**

Gastro Oesophageal Reflux Disease: Lansoprazole 30 mg gastro-resistant capsules once daily for 4 weeks. The majority of patients will be healed after the first course. For those patients not fully healed at this time, a further 4 weeks

treatment at the same dosage should be given.

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

Duodenal ulcer: Lansoprazole 30 mg gastro-resistant capsules once daily for 4 weeks.

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

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

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

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

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

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

For patients who require 120mg 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 before a meal. 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 capsules 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 30mg are administered to patients with severe hepatic impairment. It is therefore recommended that the daily dose for patients with severe liver disease is

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

There is no need to alter the dosage in patients with mild to moderate impairment of hepatic function or impaired renal function.

#### **4.3 Contraindications**

The use of lansoprazole is contra-indicated in patients with a history of hypersensitivity to any of the ingredients of Lansoprazole 15mg or 30 mg gastro-resistant 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 medicine contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

#### **4.5 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 15mg or 30 mg gastro-resistant capsules.

#### **4.6 Pregnancy and lactation**

There is insufficient experience to recommend the use of lansoprazole in

pregnancy. Animal studies do not reveal any teratogenic effect. Reproduction studies indicate slightly reduced litter survival and weights in rats and rabbits given very high doses of lansoprazole.

The use of lansoprazole in pregnancy should be avoided.

Animal studies indicate that lansoprazole is secreted in breast milk.

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

#### **4.7 Effects on ability to drive and use machines**

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

#### **4.8 Undesirable effects**

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

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

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

As with other PPIs, very rarely, cases of colitis have been reported.

In severe and/or protracted cases of diarrhoea, discontinuation of therapy should be considered. In the majority of cases symptoms resolve on discontinuation of therapy.

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

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

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

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

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

Gynaecomastia and impotence have been reported rarely.

#### 4.9 Overdose

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

### 5. PHARMACOLOGICAL PROPERTIES

#### 5.1. Pharmacodynamic properties

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 sulphhydryl group of the  $H^+ / K^+$  ATPase causing inhibition. This inhibition is reversible *in vitro* by intrinsic and extrinsic reducing agents. Lansoprazole's mode of action differs significantly from the  $H_2$  antagonists which inhibit one of the three pathways involved in stimulation of acid production. A single dose of 30mg inhibits pentagastrin-stimulated acid secretion by approximately 80%, indicating effective acid inhibition from the first day of dosing.

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

By reducing gastric acidity, Lansoprazole 15, 30 mg capsules creates an environment in which appropriate antibiotics can be effective against *H. pylori*. *In vitro* studies have shown that lansoprazole has a direct antimicrobial effect on *H. pylori*.

#### 5.2. Pharmacokinetic properties

Lansoprazole exhibits high (80-90%) bioavailability with a single dose. As a result, effective acid inhibition is achieved rapidly. Peak plasma levels occurred within 1.5 to 2.0 hours. The plasma elimination half-life ranges from 1 to 2 hours following single or multiple doses in healthy subjects. There is no evidence of accumulation following multiple doses in healthy subjects. The plasma protein binding is 97%.

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

#### 5.3. Preclinical safety data

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

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

### 6. PHARMACEUTICAL PARTICULARS

**6.1 List of excipient(s)**

**Capsule contents:** Hypromellose (E-464), Talc (E-553b), Titanium dioxide (E-171), Metacrylic acid-ethyl acrylate copolymer (1:1) dispersion 30%, Triethylcitrate (E-1505), Sugar spheres (sucrose and maize starch)

**Capsule Shells:** Titanium dioxide (E-171), Purified water, Gelatine.

**Printing ink:** shellac and black iron oxide (E-172).

**6.2 Incompatibilities**

Not applicable.

**6.3 Shelf-life**

Bottle (HDPE): 24 months. In-use stability has been demonstrated for 28 days

Blister (Al/Al): 24 months

**6.4 Special precautions for storage**

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

Bottle pack: Do not store above 25 °C. Keep the bottle tightly closed to protect from moisture.

**6.5 Nature and contents of container**

Bottle packs: HDPE container and screw cap with tamper evident ring containing a desiccant capsule (LDPE)

Bottles of 7, 14, 28 and 56 (28x2) capsules

Blister packs: Al/Al foil. Each blister strip contains 7 capsules.

Blister packs of 7 (1 blister strip), 14 (2 blister strips), 28 (4 blister strips), 42 (6 blister strips) and 56 (8 blister strips) capsules

Not all pack sizes may be marketed

**6.6 Instructions for use and handling**

No special requirements.

**7. MARKETING AUTHORISATION HOLDER**

Dexter Farmacéutica, S.A.

Avda. Mare de Déu de Montserrat, 215

08041 Barcelona

Spain

**8. MARKETING AUTHORISATION NUMBER**

PL 21561/0002

**9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

06/12/2005

**10**    **DATE OF REVISION OF THE TEXT**  
06/12/2005

**5. POSSIBLE SIDE EFFECTS**

Like all medicines, lansoprazole can have side effects.

**If you experience any of the following, stop taking your medicine and tell your doctor immediately or go straight to the casualty department at your nearest hospital:**

- An allergic reaction consisting of swelling of the hands, feet, ankles, face, lips or throat which may cause difficulty breathing or swallowing, itching of the skin and nettle rash.
  - Stevens-Johnson syndrome (blisters/bleeding of the lips, eyes, nose mouth and genitals)
  - A severe blistering rash in which layers of the skin may peel off to leave large areas of raw, exposed skin over the body.
  - Inflammation of the liver or changes in your liver function. This may result in symptoms such as: yellowing of your skin or whites of your eyes, tiredness and fever.
  - Kidney problems or changes in your kidney function which may lead to difficulties in urinating.
  - Reddening or blistering of your skin.
  - Blood disorders which may result in abnormal bruising or bleeding
- While these are serious side effects that require urgent medical attention, they are very rare.

The natural acid in your stomach helps to kill bacteria. Taking medicines like lansoprazole that 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).

As with other proton pump inhibitors, men taking lansoprazole may experience breast swelling or impotence. This is, however, very unlikely to happen to you.

The milder side effects of lansoprazole are: headaches, dizziness, tiredness, a general feeling of being unwell, diarrhoea, constipation, stomach pain, feelings of sickness, being sick (vomiting), dry or sore mouth and throat, rash/itching, hair thinning, sensitivity to light, muscle or joint pain, depression, swelling of the hands and feet, pins and needles, blurred vision, changes in the way things taste, vertigo, confusion, and hallucinations.

Do not be alarmed by this list. Most people take lansoprazole without any problems. If you experience these or any other unusual side effects not mentioned in this leaflet, please contact your doctor or pharmacist as soon as possible. If your symptoms are severe or last for more than a few days, contact your doctor immediately.

Before you have any kind of surgery, tell the doctor in charge that you are taking lansoprazole

**6. STORING LANSOPRAZOLE CAPSULES**

Keep your medicine out of the reach and sight of children.

Blister A/A: Do not store above 25°C. Store in the original package.

Do not use this medicine after the expiry date printed on the pack.

This leaflet does not contain all the information about your medicine. If you have any questions or are not sure about anything, ask your doctor or pharmacist.

This leaflet was last revised in November 2005.

EA 3927-05-7-Ag

**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 only 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.
- Your doctor may have given you this medicine before from another company and it may have looked slightly different. Either brand will have the same effect.

**In this leaflet**

1. What Lansoprazole Capsules are
2. What Lansoprazole Capsules are used for
3. Before you take Lansoprazole Capsules
4. How to take Lansoprazole Capsules
5. Possible side effects
6. Storing Lansoprazole Capsules

**1. WHAT LANSOPRAZOLE CAPSULES ARE**

The name of this medicine is Lansoprazole 15 & 30 mg gastro-resistant capsules (referred to as lansoprazole throughout this leaflet).

Each gastro-resistant capsule contains 15 mg or 30 mg lansoprazole. The other ingredients are: hypromellose (E-464), talc (E-553b), titanium dioxide (E-171), metacrylic acid-ethyl acrylate copolymer (1:1) dispersion 30 %, triethylcitrate (E-1505), sugar spheres (sucrose and maize starch), gelatine and black ink (shellac and Black Iron Oxide (E-172)).

**The Marketing Authorisation holder is:** Dexter Farmacéutica, S.A. Avda. Mare de Déu de Montserrat, 215, 08041 Barcelona (Spain)

**The Manufacturer is:** Laboratorios Dr. Esteve S.A., Sant Martí, s/n, Polígono Industrial la Roca, 08107, Martorelles, Barcelona, Spain.

The gastro-resistant capsules are white and imprinted with LAN 15 and LAN 30 for Lansoprazole 15 mg gastro-resistant capsules and Lansoprazole 30 mg gastro-resistant capsules respectively.

The 15 mg capsules come in blister packs of 28 and 56 capsules.

The 30 mg capsules come in blister packs of 28 and 56 capsules.

**2. WHAT LANSOPRAZOLE CAPSULES ARE USED FOR**

Lansoprazole belongs to a group of medicines called proton pump inhibitors (pharmaco-therapeutic group A02BC). It reduces the production of acid in your stomach.

Your doctor has prescribed lansoprazole for you to treat one of the following conditions:

- Heal ulcers in your stomach or duodenum, 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 (shortened to GORD).
  - Give you relief from the unpleasant symptoms that often occur with these conditions.
  - Stop these conditions coming back.

It is sometimes given to stop you getting an ulcer while you are taking an NSAID.

It also takes away the pain of heartburn or indigestion and other unpleasant symptoms that can occur with the condition known as acid-related dyspepsia. It is sometimes given to patients whose stomachs make too much acid. This includes a condition called Zollinger-Ellison syndrome.

### 3. BEFORE YOU TAKE LANSOPRAZOLE CAPSULES

**Do not take lansoprazole if you:**

Are allergic to lansoprazole or any of the other ingredients in the capsules.

**Special care is needed (check with your doctor) if you:**

Have 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**

You should not take lansoprazole if you are pregnant, think you are pregnant, planning a pregnancy or if you are breast-feeding. Speak to your doctor or pharmacist for advice.

**Driving and using machines**

Lansoprazole does not usually affect your ability to drive. However, if you experience dizziness, headache, tiredness, nausea or problems with your vision do not drive or operate machinery, as they may affect your ability to react.

**Taking other medicines**

If taken with some other medicines the effects of lansoprazole or the effects of other medicines may be changed. Please check with your doctor if you are taking any of the following:

- the contraceptive pill
- theophylline which is 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

Please consult your doctor, even if these statements were applicable to you at any time in the past or if you are taking, or have recently taken, any other medicine – even those not prescribed.

### 4. HOW TO TAKE LANSOPRAZOLE CAPSULES

Your doctor will tell you how to take your medicine. The actual dose of lansoprazole depends on your needs and the condition being treated but the usual doses for adults are listed below:

**HEALING OF STOMACH ULCERS**

One 30 mg gastro-resistant capsule every day for 8 weeks.

**DUODENAL ULCERS**

One 30 mg gastro-resistant capsule every day for 4 weeks to heal it then, if your doctor decides you need it, one 15 mg gastro-resistant capsule every day to stop it coming back.

**STOMACH AND DUODENAL ULCERS CAUSED BY AN NSAID**

One 15 mg or 30 mg gastro-resistant capsule every day for 4 or 8 weeks to heal it then, if your doctor decides you need it, one 15 mg or 30 mg gastro-resistant capsule every day for as long as your doctor decides you need to take lansoprazole to stop the ulcer or your symptoms coming back

**PREVENTION OF AN ULCER AND RELIEF OF SYMPTOMS WHILE YOU TAKE AN NSAID**

One 15 mg or 30 mg gastro-resistant capsule every day for as long as your doctor decides you need to take lansoprazole for.

**GASTRO-OESOPHAGEAL REFLUX DISEASE**

One 30 mg gastro-resistant capsule a day for 4 to 8 weeks to heal your oesophagus and/or relieve symptoms then, if your doctor decides you need it, one 15 mg or 30 mg gastro-resistant capsule a day to stop your condition coming back

**ACID-RELATED DYSPEPSIA**

One 15 mg or 30 mg gastro-resistant capsule every day for 2 to 4 weeks. Go back to your doctor if your symptoms do not get better after this time or return soon after you have completed the course.

**CONDITIONS WHERE YOUR STOMACH MAKES TOO MUCH ACID LIKE ZOLLINGER-ELLISON SYNDROME**

Two 30 mg gastro-resistant capsules every day to start with then, depending how you respond to lansoprazole, take the dose that your doctor decides is best for you.

**Patients with liver problems**

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

**Children**

Lansoprazole is not recommended for treatment in children.

**Taking your medicine**

Swallow your capsules whole with a glass of water. Do not crush or chew as this will stop them from working properly.

If you are taking lansoprazole once a day, take it at the same time each morning before breakfast.

If you are taking lansoprazole twice a day, take the first dose in the morning before breakfast and the second dose in the evening.

**If you take more lansoprazole than you should:**

An overdose of this medicine may be dangerous. If you or someone else has taken too many capsules tell your doctor or go to the nearest hospital casualty department immediately.

**If you forget to take lansoprazole:**

If you forget to take a dose at the right time, take it as soon as you remember, then go on as before. Do not try to make up for the missed dose by taking two doses at the same time.

**Effects when treatment with lansoprazole is stopped:**

Keep taking your medicine until your doctor tells you to stop. Do not stop taking lansoprazole just because you feel better. If you stop them, your condition may get worse



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- Give you relief from the unpleasant symptoms that often occur with these conditions.

• Stop these conditions coming back.

It is sometimes given to stop you getting an ulcer while you are taking an NSAID.

It also takes away the pain of heartburn or indigestion and other unpleasant symptoms that can occur with the condition known as acid-related dyspepsia. It is sometimes given to patients whose stomachs make too much acid. This includes a condition called Zollinger-Ellison syndrome.

**3. BEFORE YOU TAKE LANSOPRAZOLE CAPSULES****Do not take lansoprazole if you:**

- Are allergic to lansoprazole or any of the other ingredients in the capsules.

**Special care is needed (check with your doctor) if you:**

- Have 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**

You should not take lansoprazole if you are pregnant, think you are pregnant, planning a pregnancy or if you are breast-feeding. Speak to your doctor or pharmacist for advice.

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Lansoprazole does not usually affect your ability to drive. However, if you experience dizziness, headache, tiredness, nausea or problems with your vision do not drive or operate machinery, as they may affect your ability to react.

**Taking other medicines**

If taken with some other medicines the effects of lansoprazole or the effects of other medicines may be changed. Please check with your doctor if you are taking any of the following:

- the contraceptive pill
- theophylline which is 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

Please consult your doctor, even if these statements were applicable to you at any time in the past or if you are taking, or have recently taken, any other medicine – even those not prescribed.

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One 30 mg gastro-resistant capsule every day for 4 weeks to heal it then, if your doctor decides you need it, one 15 mg gastro-resistant capsule every day to stop it coming back.

**STOMACH AND DUODENAL ULCERS CAUSED BY AN NSAID**

One 15 mg or 30 mg gastro-resistant capsule every day for 4 or 8 weeks to heal it then, if your doctor decides you need it, one 15 mg or 30 mg gastro-resistant capsule every day for as long as your doctor decides you need to take lansoprazole to stop the ulcer or your symptoms coming back.

**PREVENTION OF AN ULCER AND RELIEF OF SYMPTOMS WHILE YOU TAKE AN NSAID**

One 15 mg or 30 mg gastro-resistant capsule every day for as long as your doctor decides you need to take lansoprazole for.

**GASTRO-OESOPHAGEAL REFLUX DISEASE**

One 30 mg gastro-resistant capsule a day for 4 to 8 weeks to heal your oesophagus and/or relieve symptoms then, if your doctor decides you need it, one 15 mg or 30 mg gastro-resistant capsule a day to stop your condition coming back.

**ACID-RELATED DYSPEPSIA**

One 15 mg or 30 mg gastro-resistant capsule every day for 2 to 4 weeks. Go back to your doctor if your symptoms do not get better after this time or return soon after you have completed the course.

**CONDITIONS WHERE YOUR STOMACH MAKES TOO MUCH ACID LIKE ZOLLINGER-ELLISON SYNDROME**

Two 30 mg gastro-resistant capsules every day to start with then, depending how you respond to lansoprazole, take the dose that your doctor decides is best for you.

**Patients with liver problems**

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

**Children**

Lansoprazole is not recommended for treatment in children.

**Taking your medicine**

Swallow your capsules whole with a glass of water. Do not crush or chew as this will stop them from working properly.

If you are taking lansoprazole once a day, take it at the same time each morning before breakfast.

If you are taking lansoprazole twice a day, take the first dose in the morning before breakfast and the second dose in the evening.

**If you take more lansoprazole than you should:**

An overdose of this medicine may be dangerous. If you or someone else has taken too many capsules tell your doctor or go to the nearest hospital casualty department immediately.

**If you forget to take lansoprazole:**

If you forget to take a dose at the right time, take it as soon as you remember, then go on as before. Do not try to make up for the missed dose by taking two doses at the same time.

**Effects when treatment with lansoprazole is stopped:**

Keep taking your medicine until your doctor tells you to stop. Do not stop taking lansoprazole just because you feel better. If you stop them, your condition may get worse.

**5. POSSIBLE SIDE EFFECTS**

Like all medicines, lansoprazole can have side effects.

**If you experience any of the following, stop taking your medicine and tell your doctor immediately or go straight to the casualty department at your nearest hospital:**

- An allergic reaction consisting of swelling of the hands, feet, ankles, face, lips or throat which may cause difficulty breathing or swallowing, itching of the skin and nettle rash.
- Stevens-Johnson syndrome (blisters/bleeding of the lips, eyes, nose mouth and genitals)
- A severe blistering rash in which layers of the skin may peel off to leave large areas of raw, exposed skin over the body.
- Inflammation of the liver or changes in your liver function. This may result in symptoms such as: yellowing of your skin or whites of your eyes, tiredness and fever.
- Kidney problems or changes in your kidney function which may lead to difficulties in urinating.
- Reddening or blistering of your skin.
- Blood disorders which may result in abnormal bruising or bleeding

While these are serious side effects that require urgent medical attention, they are very rare.

The natural acid in your stomach helps to kill bacteria. Taking medicines like lansoprazole that 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).

As with other proton pump inhibitors, men taking lansoprazole may experience breast swelling or impotence. This is, however, very unlikely to happen to you.

The milder side effects of lansoprazole are: headache, dizziness, tiredness, a general feeling of being unwell, diarrhoea, constipation, stomach pain, feelings of sickness, being sick (vomiting), dry or sore mouth and throat, rash/itching, hair thinning, sensitivity to light, muscle or joint pain, depression, swelling of the hands and feet, pins and needles, blurred vision, changes in the way things taste, vertigo, confusion, and hallucinations.

Do not be alarmed by this list. Most people take lansoprazole without any problems. If you experience these or any other unusual side effects not mentioned in this leaflet, please contact your doctor or pharmacist as soon as possible. If your symptoms are severe or last for more than a few days, contact your doctor immediately.

Before you have any kind of surgery, tell the doctor in charge that you are taking lansoprazole.

**6. STORING LANSOPRAZOLE CAPSULES**

Keep your medicine out of the reach and sight of children.

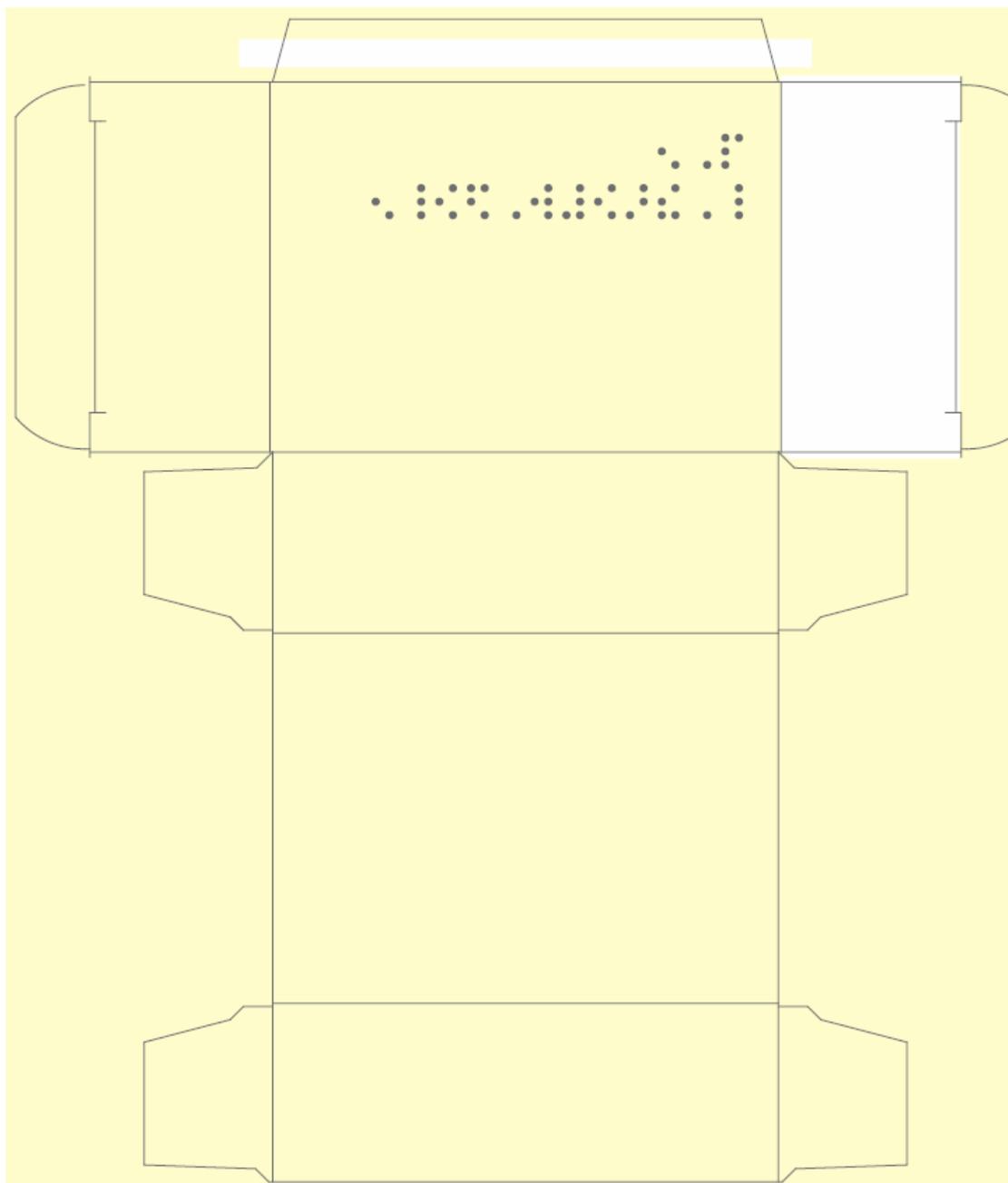
Do not store above 25°C. Keep the bottle tightly closed to protect from moisture.

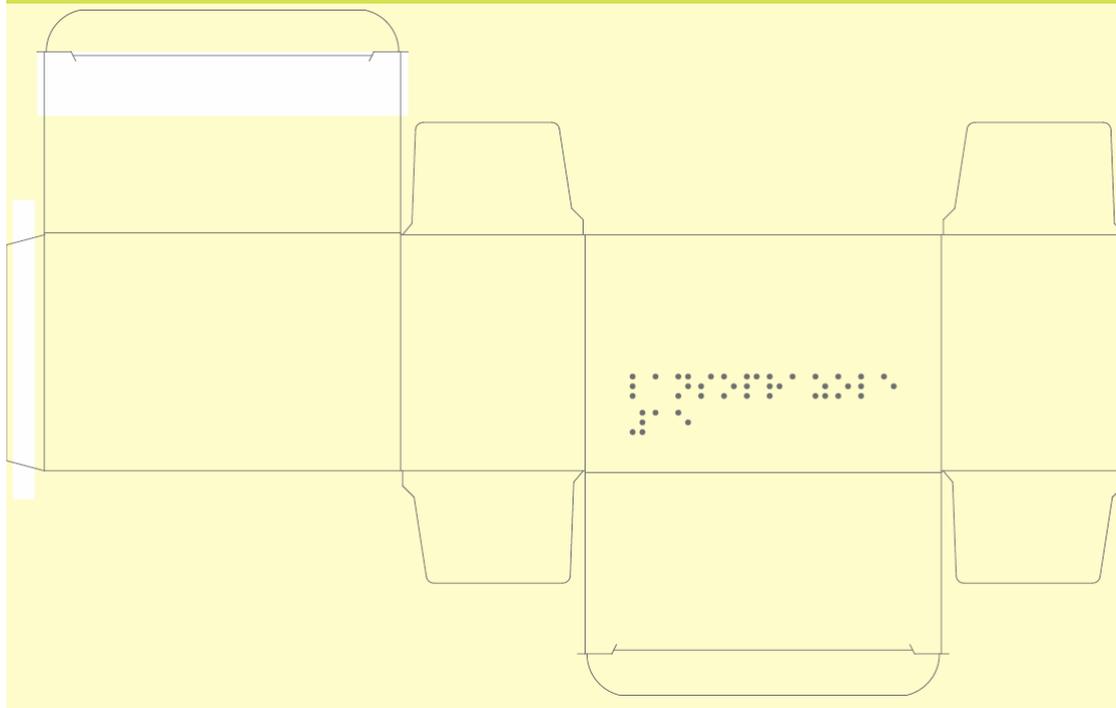
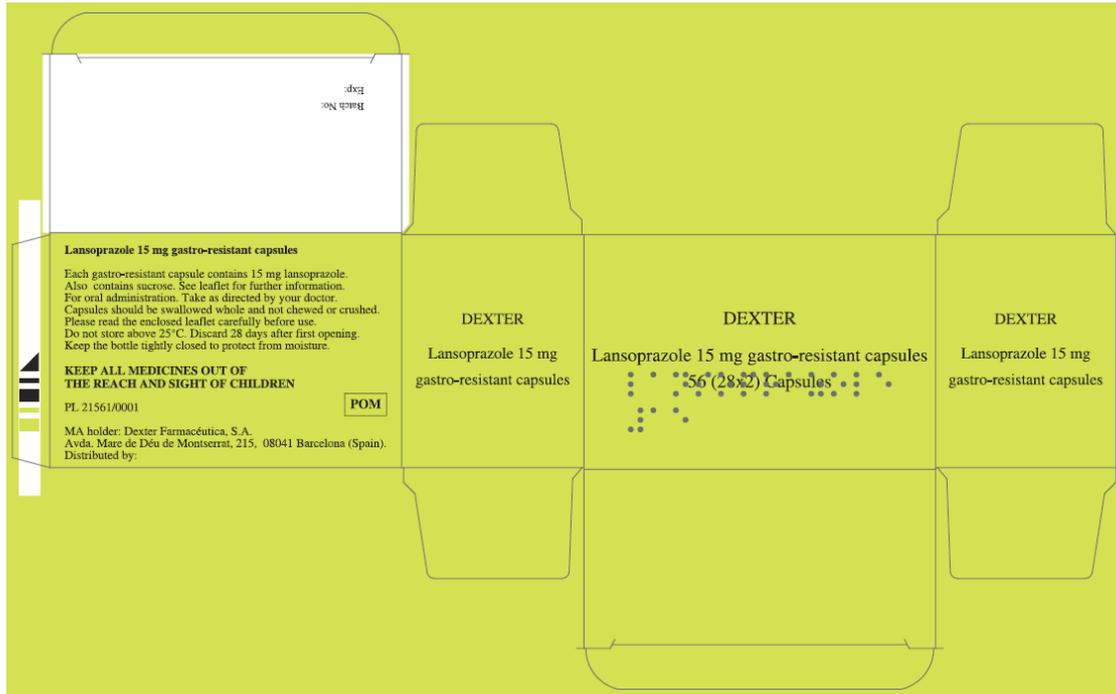
Do not use this medicine after the expiry date printed on the pack. Any capsules remaining 28 days after first opening should either be discarded safely or returned to your pharmacist. This leaflet does not contain all the information about your medicine. If you have any questions or are not sure about anything, ask your doctor or pharmacist.

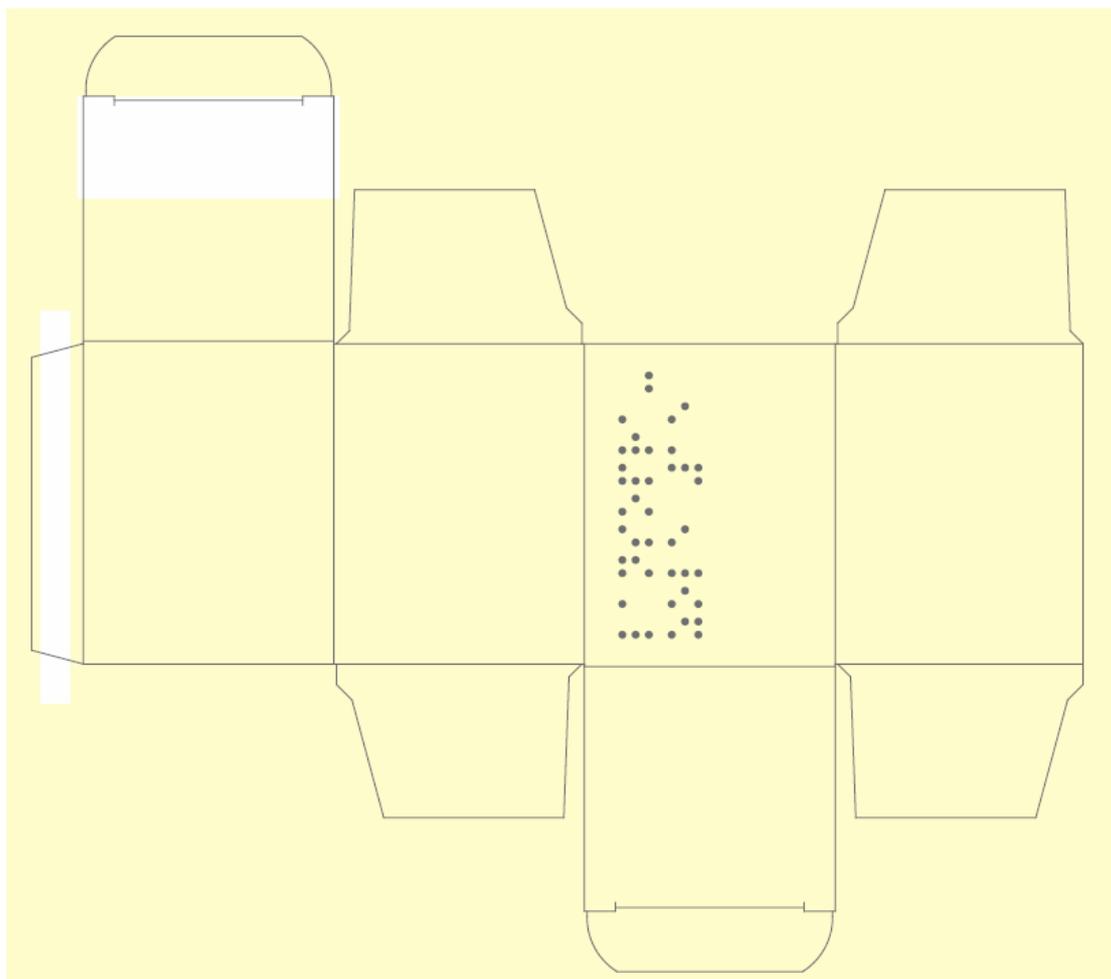
This leaflet was last revised in November 2005.

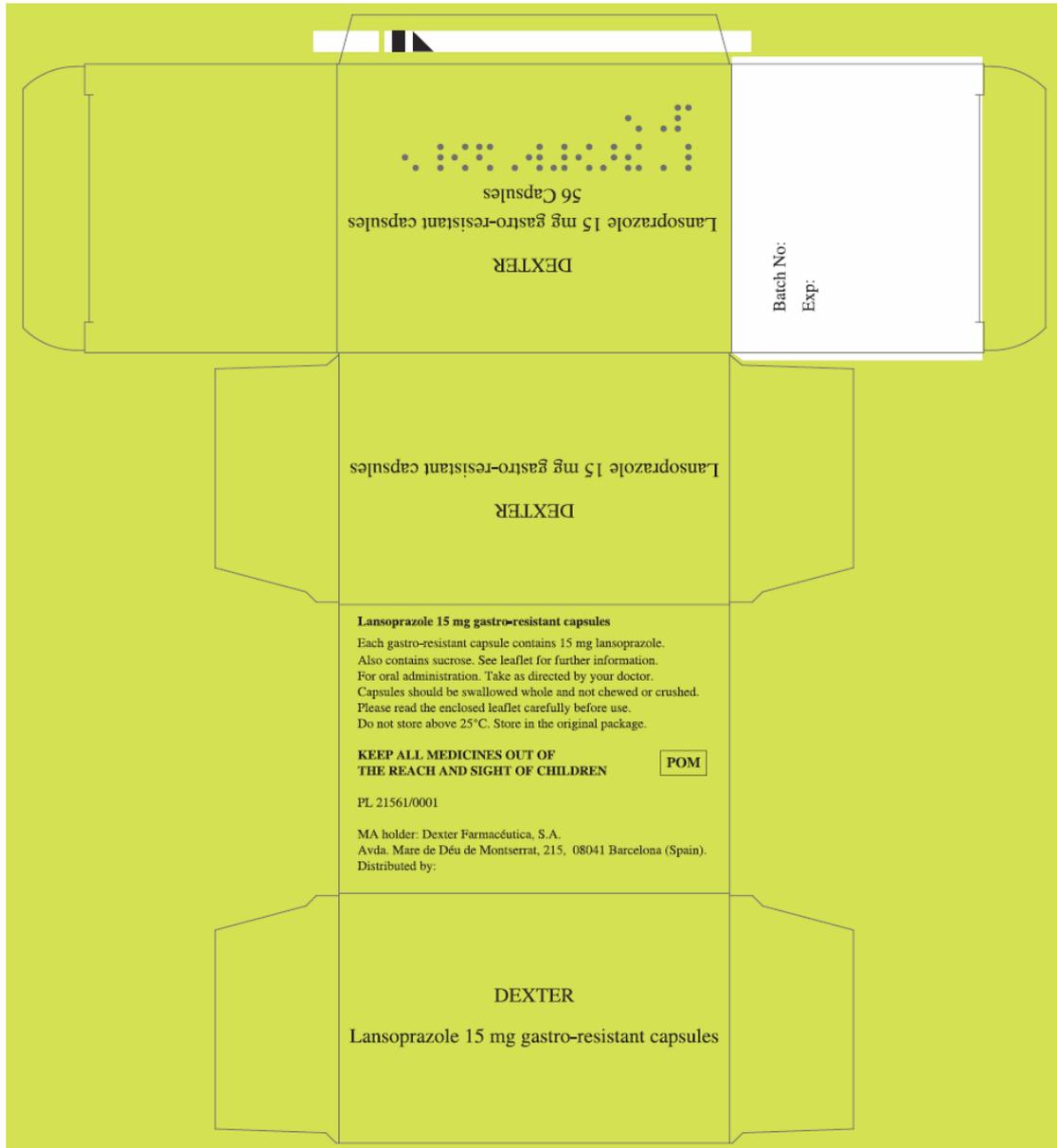
**Lansoprazole 15mg Capsules**

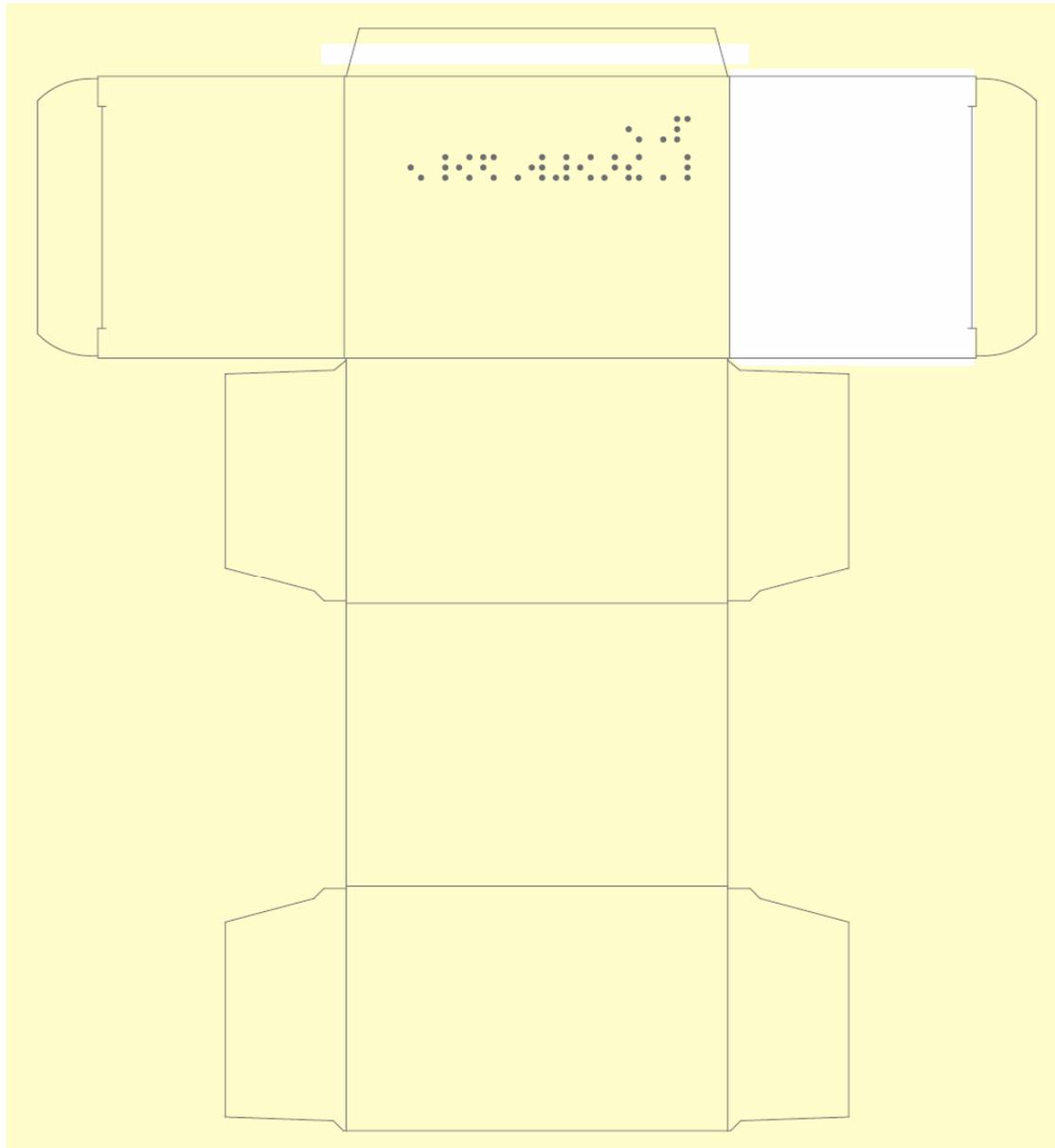












**DEXTER Lansoprazole 15 mg gastro-resistant capsules**  
 Each gastro-resistant capsule contains 15 mg lansoprazole. Also contains sucrose. See leaflet for further information. For oral administration. Take as directed by your doctor. Capsules should be swallowed whole and not chewed or crushed. Please read the enclosed leaflet carefully before use. Discard 28 days after first opening. Do not store above 25°C. Keep the bottle tightly closed to protect from moisture.

P. 21561/0001  
 MA holder: Dexter Farmaceutica, S.A.  
 Avda. Meritxè de Oteiza de Montoliu, 215,  
 08041 Barcelona (Spain).  
 Distributed by:

KEEP ALL MEDICINES OUT OF THE REACH AND SIGHT OF CHILDREN

**15 mg**  
**28 CAPSULES**

BATCH  
 EXP. DATE

**DEXTER Lansoprazole 15 mg gastro-resistant capsules**  
 Each gastro-resistant capsule contains 15 mg lansoprazole. Also contains sucrose. See leaflet for further information. For oral administration. Take as directed by your doctor. Capsules should be swallowed whole and not chewed or crushed. Please read the enclosed leaflet carefully before use. Discard 28 days after first opening. Do not store above 25°C. Keep the bottle tightly closed to protect from moisture.

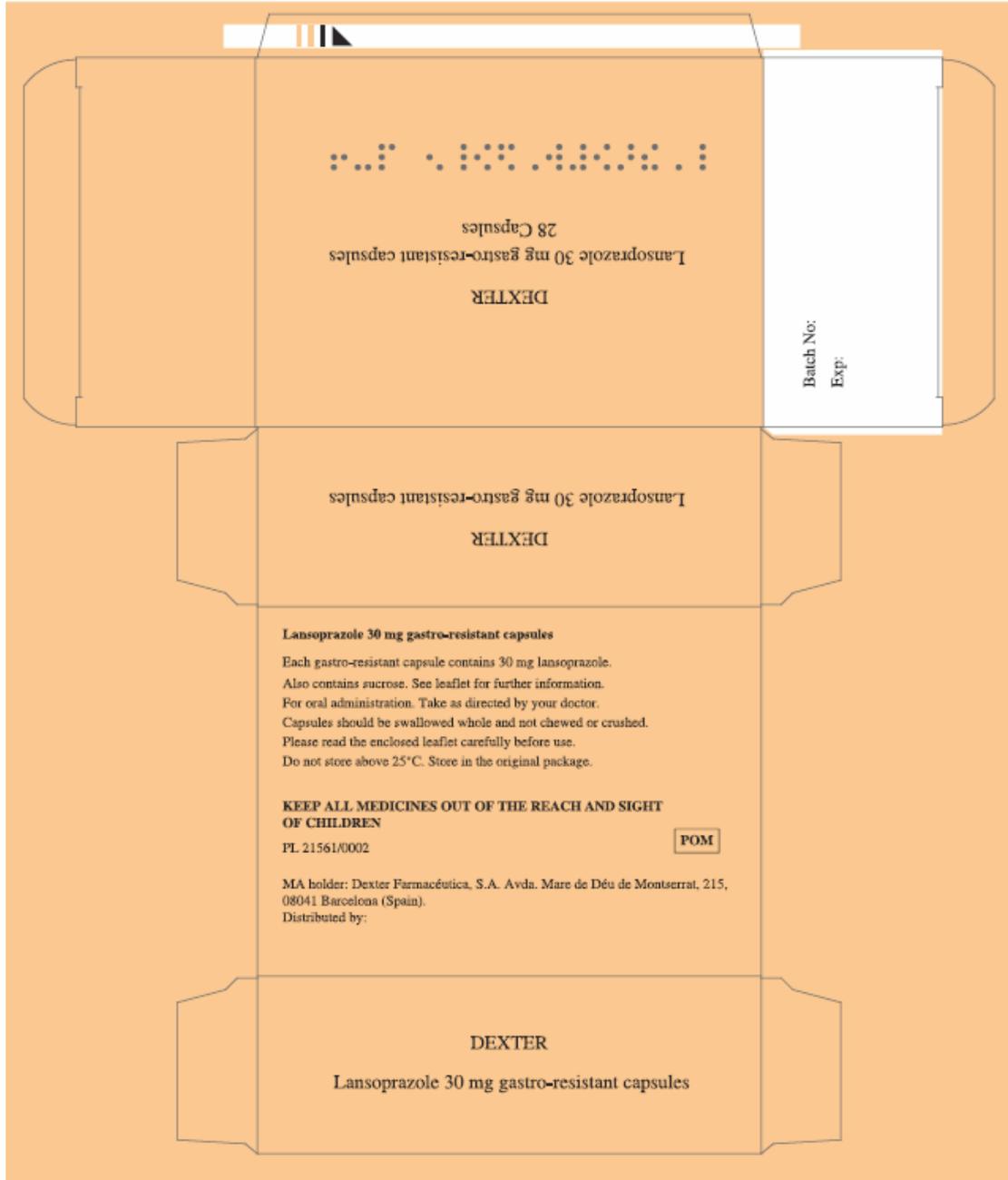
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 MA holder: Dexter Farmaceutica, S.A.  
 Avda. Meritxè de Oteiza de Montoliu, 215,  
 08041 Barcelona (Spain).  
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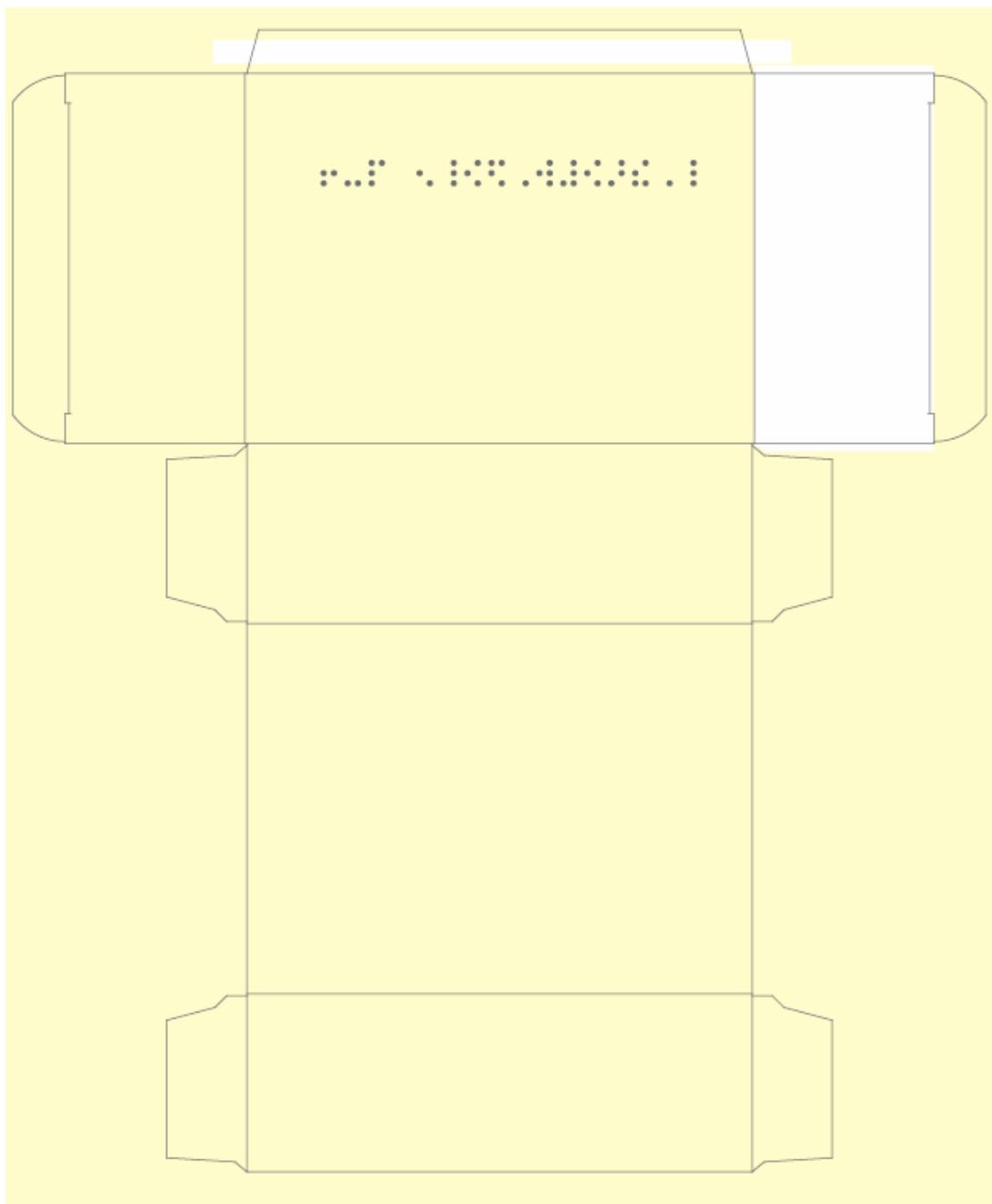
KEEP ALL MEDICINES OUT OF THE REACH AND SIGHT OF CHILDREN

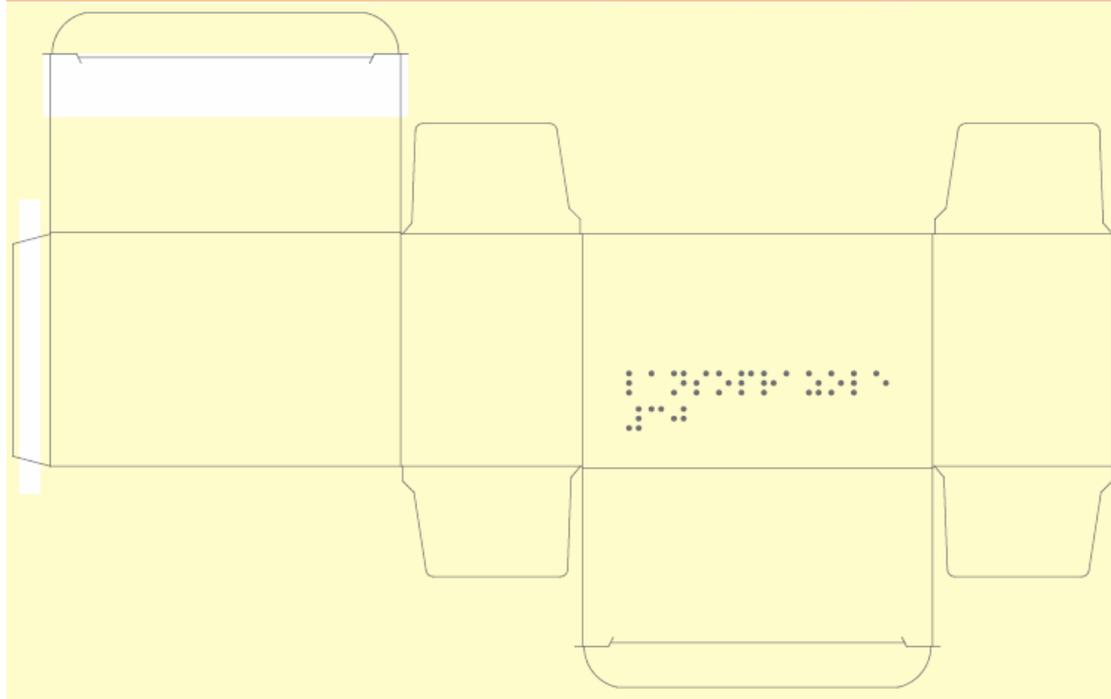
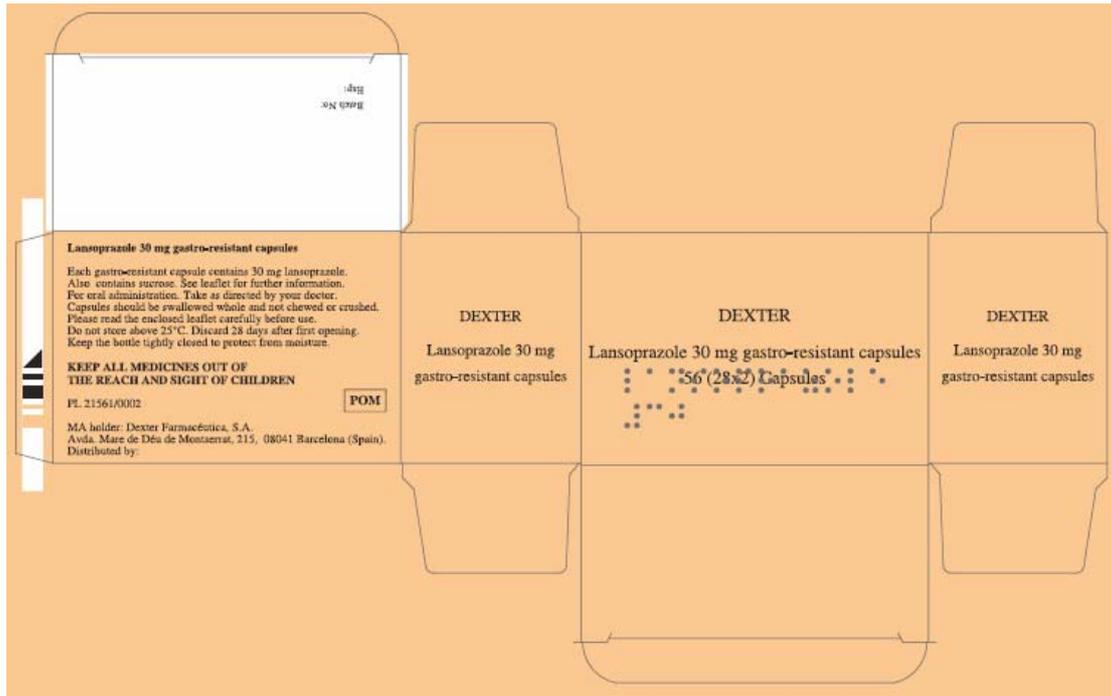
**15 mg**  
**28 CAPSULES**  
 (part of a packaging of 56)

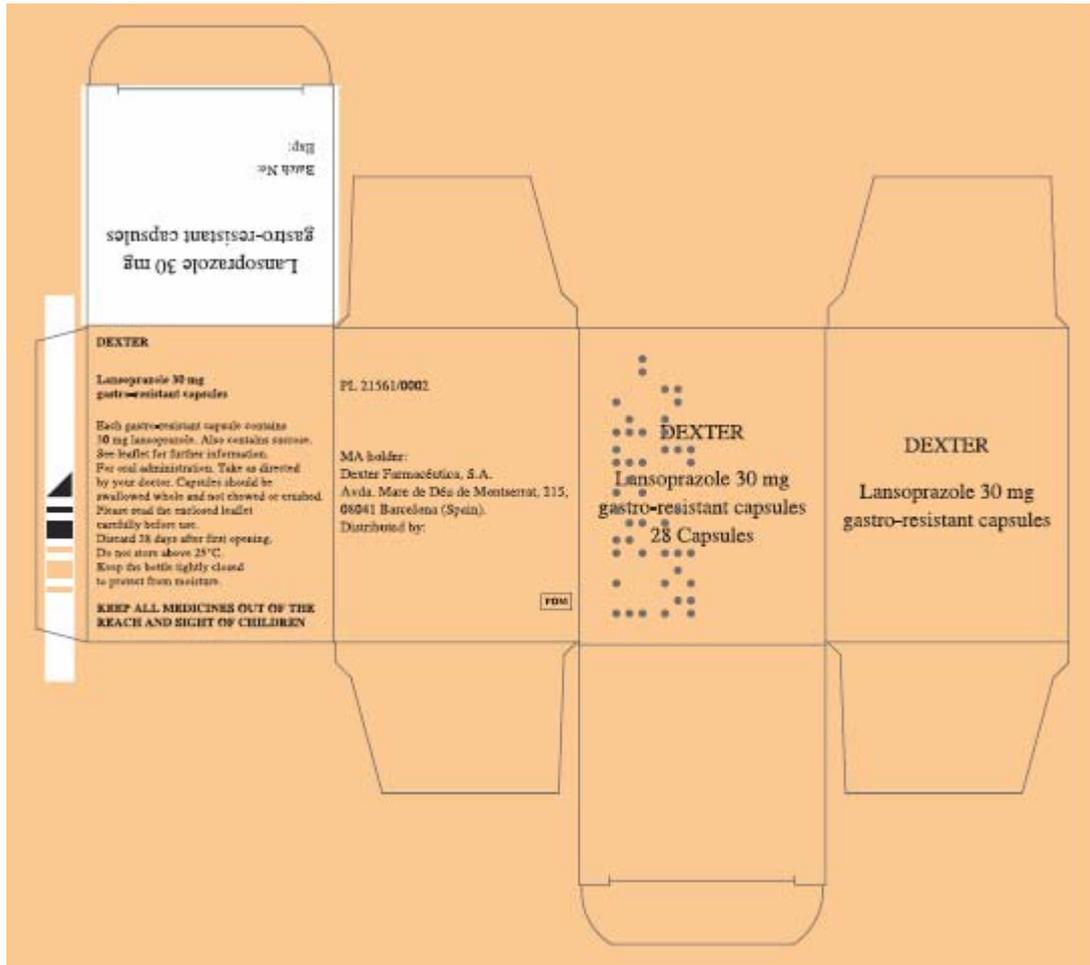
BATCH  
 EXP. DATE

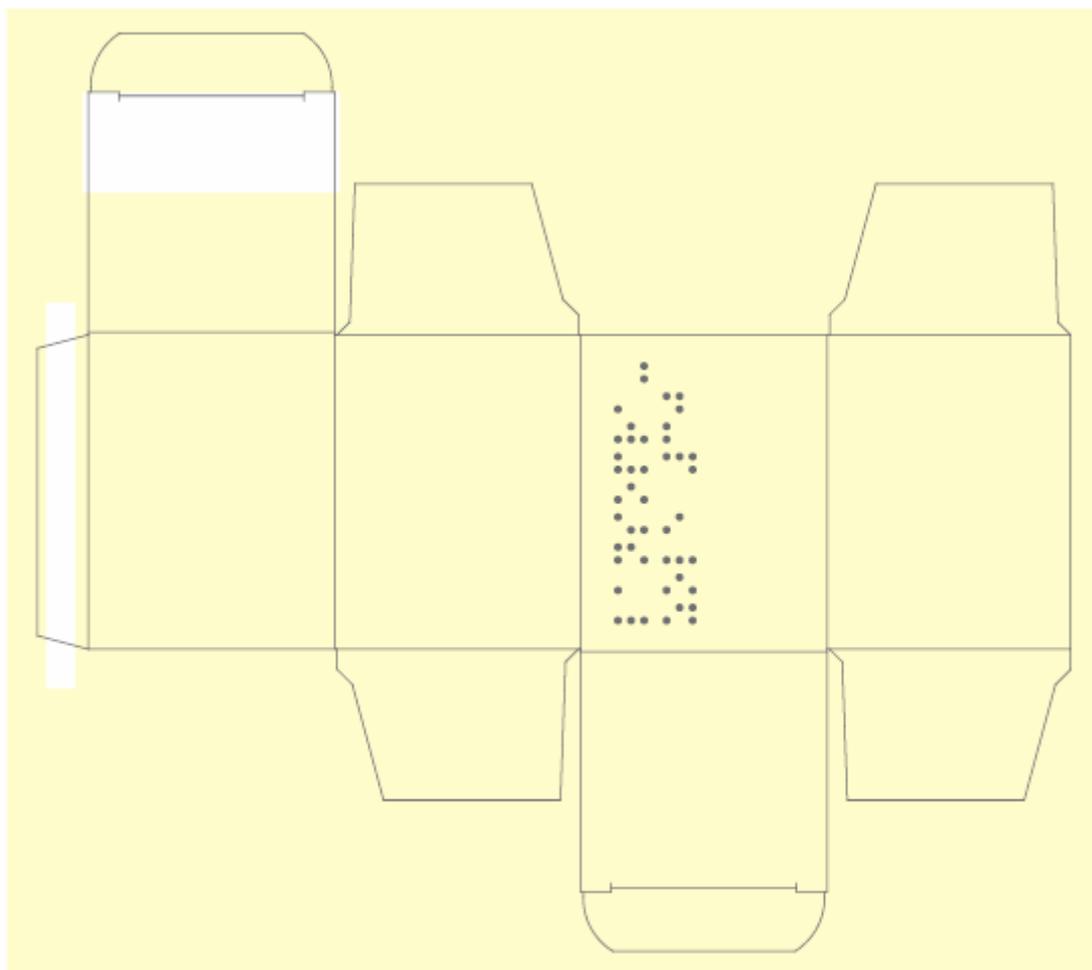
**Lansoprazole 30mg Capsules**

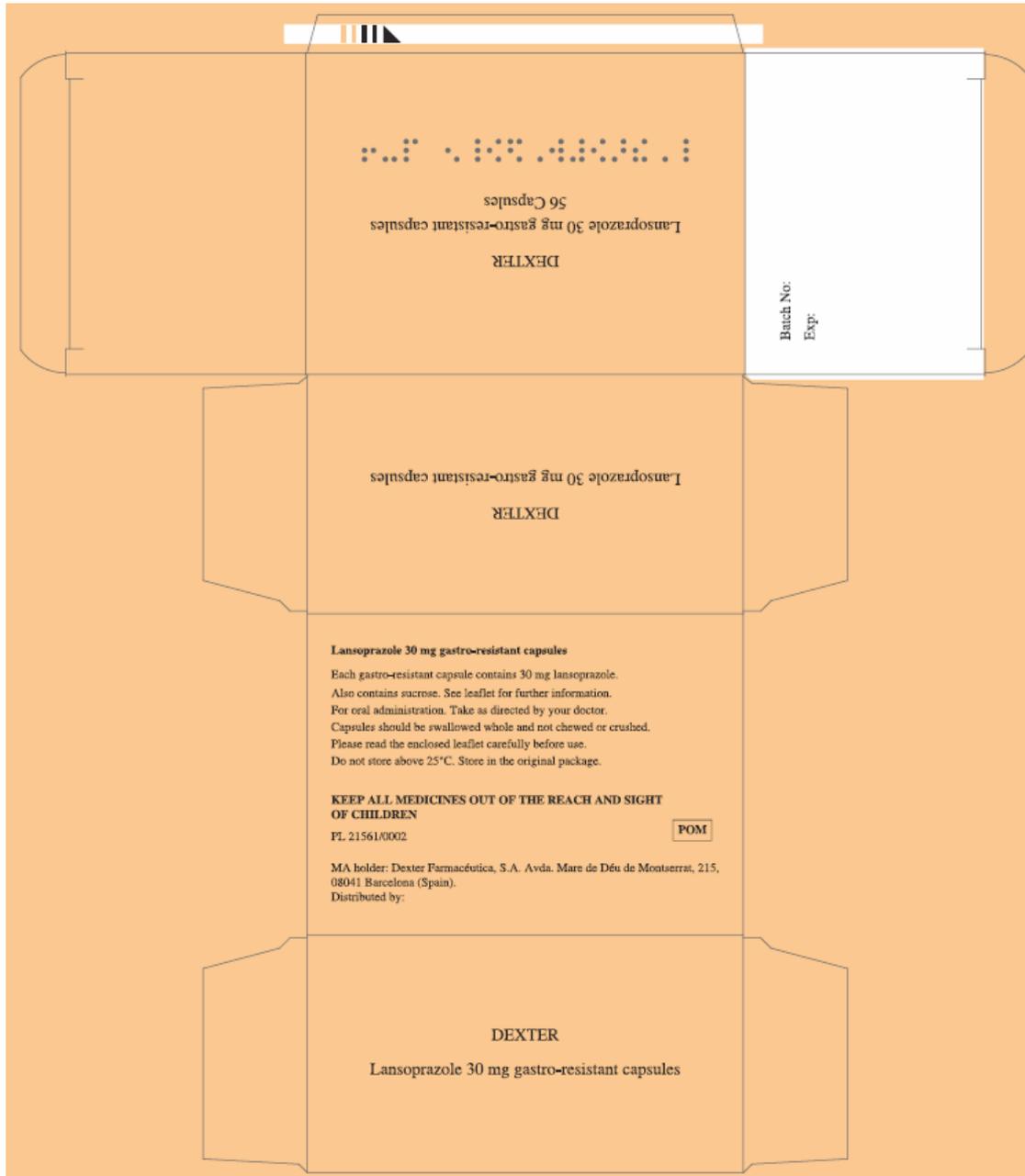


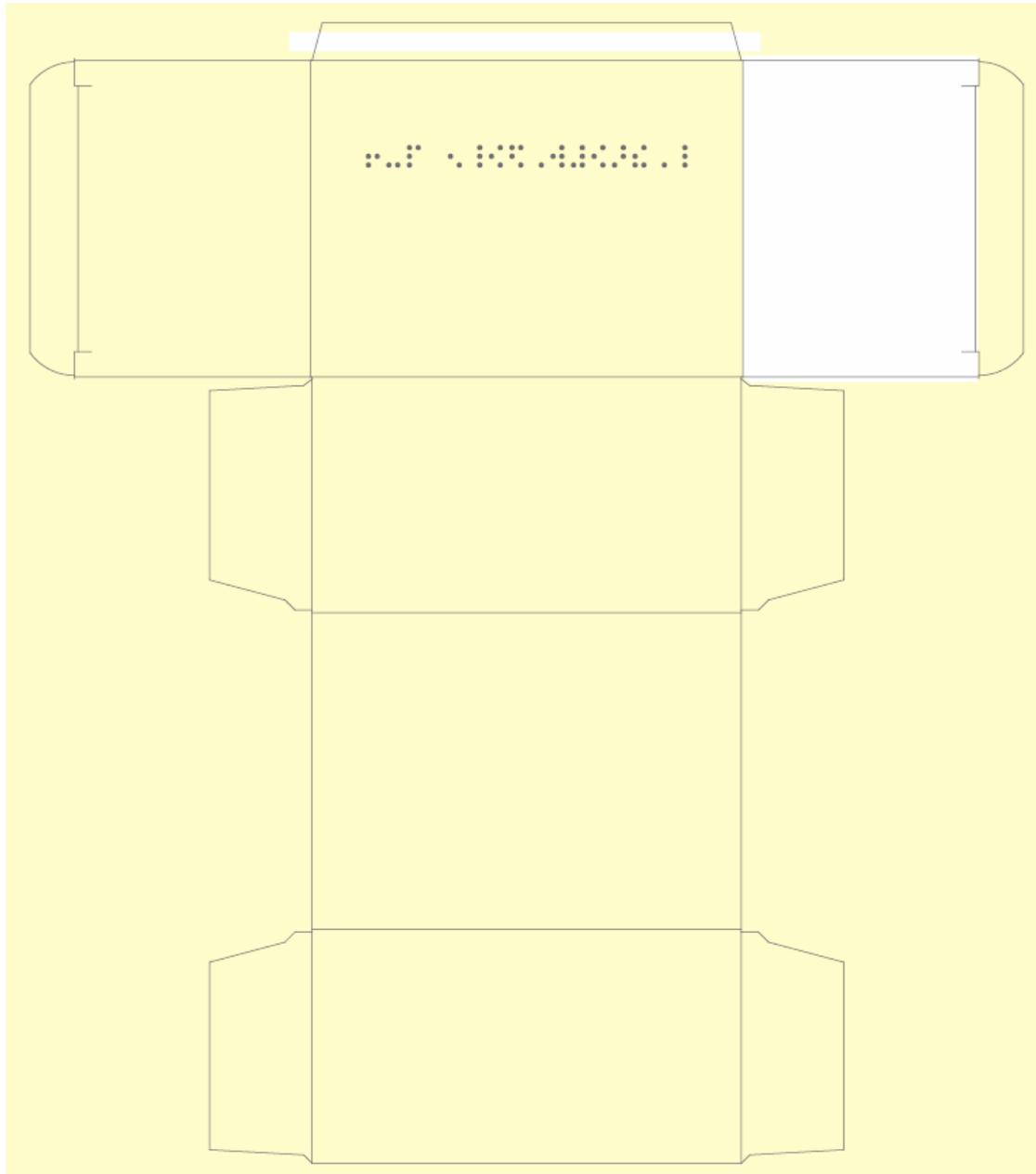












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| <p><b>DEXTER Lansoprazole 30 mg gastro-resistant capsules</b><br/>                 Each gastro-resistant capsule contains 30 mg lansoprazole. Also contains sucrose. See leaflet for further information. For oral administration. Take as directed by your doctor. Capsules should be swallowed whole and not chewed or crushed. Please read the enclosed leaflet carefully before use. Discard 28 days after first opening. Do not store above 25°C. Keep the bottle tightly closed to protect from moisture.</p> | <p>PL 21561/0002<br/>                 MA Ind. Dex: Dexter Farmacolico, S.A.<br/>                 Avda. Mare de Déu de Montserrat, 215,<br/>                 08041 Sant Joan de Vilatorrada (Spain).<br/>                 Distributed by:</p> | <p>KEEP ALL MEDICINES OUT OF THE REACH AND SIGHT OF CHILDREN<br/> <b>30 mg</b><br/> <b>28 CAPSULES</b><br/>                 (part of a packaging of 84)</p> | <p>BATCH<br/>                 EXP. DATE</p> |
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|   |  |  |   |
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| <p><b>DEXTER Lansoprazole 30 mg gastro-resistant capsules</b><br/>                 Each gastro-resistant capsule contains 30 mg lansoprazole. Also contains sucrose. See leaflet for further information. For oral administration. Take as directed by your doctor. Capsules should be swallowed whole and not chewed or crushed. Please read the enclosed leaflet carefully before use. Discard 28 days after first opening. Do not store above 25°C. Keep the bottle tightly closed to protect from moisture.</p> | <p>PL 21561/0002<br/>                 MA Ind. Dex: Dexter Farmacolico, S.A.<br/>                 Avda. Mare de Déu de Montserrat, 215,<br/>                 08041 Sant Joan de Vilatorrada (Spain).<br/>                 Distributed by:</p> | <p>KEEP ALL MEDICINES OUT OF THE REACH AND SIGHT OF CHILDREN<br/> <b>30 mg</b><br/> <b>28 CAPSULES</b></p> | <p>BATCH<br/>                 EXP. DATE</p> |
|---|--|--|---|