Public Assessment Report

Lansoprazole 15mg Gastro-resistant Capsules
PL 08608/0066, 0068, 0070

Lansoprazole 30mg Gastro-resistant Capsules
PL 08608/0067, 0069, 0071
LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 08608/0066, 0068, 0070

LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0067, 0069, 0071

UKPAR

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LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 08608/0066, 0068, 0070

LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0067, 0069, 0071

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) has granted Olinka UK Limited Marketing Authorisations (licences) for the medicinal products Lansoprazole 15mg Capsules (PLs 08608/0066, 0068, 0070) / Lansoprazole 30mg Capsules (PLs 08608/0067, 0069, 0071). These are prescription only medicines [POMs] used to prevent and treat disorders arising from excess acid secretion in the upper part of the gut.

These products contain the active substance lansoprazole. Lansoprazole blocks the action of the proton pump, the last step in acid production.

The clinical data presented to the MHRA, before licensing, demonstrated that Lansoprazole 15mg and 30mg Capsules are essentially similar or equivalent to the approved products, Zoton 15mg and 30mg Capsules, and as such can be used interchangeably.

No new or unexpected safety concerns arose from these applications and it was decided that the benefits of using Lansoprazole 15mg Capsules/Lansoprazole 30mg Capsules outweigh the risks, hence Marketing Authorisations have been granted.
LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 08608/0066, 0068, 0070

LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0067, 0069, 0071

SCIENTIFIC DISCUSSION

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</table>
INTRODUCTION

Based on the review of the data on quality, safety and efficacy the UK granted marketing authorisations for the medicinal products Lansoprazole 15mg Capsules (PLs 08608/0066, 0068, 0070) and Lansoprazole 30mg Capsules (PLs 08608/0067, 0069, 0071) to Olinka UK Limited on 9 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 Zoton 15mg and 30mg Capsules.

These 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 member of a class of drugs called proton pump inhibitors. Its mode of action is to inhibit 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 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.
PHARMACEUTICAL ASSESSMENT

<table>
<thead>
<tr>
<th>PRODUCT LICENCE NOs:</th>
<th>PL 08608/0066-71</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRODUCT NAMES:</td>
<td>Lansoprazole 15mg Gastro-resistant Capsules</td>
</tr>
<tr>
<td></td>
<td>Lansoprazole 30mg Gastro-resistant Capsules</td>
</tr>
<tr>
<td>ACTIVE (S):</td>
<td>Lansoprazole</td>
</tr>
<tr>
<td>COMPANY NAME:</td>
<td>Olinka UK Ltd</td>
</tr>
<tr>
<td>LEGAL STATUS:</td>
<td>POM</td>
</tr>
</tbody>
</table>

INTRODUCTION

These are national abridged applications (1 complex, 5 standard) for gastro-resistant hard capsules containing 15mg and 30mg lansoprazole as the active ingredient. The applications were made under Article 10.1(a)(iii), first paragraph of Directive 2001/83/EC. The original products are Lanzo 15mg marketed by Wyeth Lederle Nordista AB, Denmark (granted 4 May 1994) and Ogast 30mg Gelule marketed by Takeda Laboratories, France (granted 11 December 1990) respectively. The reference products in the UK are Wyeth’s Zoton Capsules 30mg PL 00011/0287 (originally PL 00095/0264 granted 23 February 1994) & Zoton Capsules 15mg PL 00011/0288 (originally PL 00095/0302 granted 17 January 1996).

Lansoprazole is a proton pump inhibitor that reduces gastric acidity and is used to treat gastro-oesophageal reflux disease, ulcers and acid-related dyspepsia.

PRODUCT NAME, APPLICATION FORMS, SUMMARY OF PRODUCT CHARACTERISTICS, LABELLING AND LEAFLET

Satisfactory.

DRUG SUBSTANCE

An open part drug master file (DMF) and a letter of access are provided. This is a new active source, hence the complex fee. The DMF submitted is in the Common Technical Document format. The DMF holder has confirmed that the applicant would be informed of any significant changes in manufacturing process or specifications of the active ingredient likely to alter the quality or safety of the product.

General Information

Nomenclature

<table>
<thead>
<tr>
<th>INN/USAN/BAN:</th>
<th>Lansoprazole</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemical Name:</td>
<td>1H-benzimidazole, 2-[[3-methyl-4-(2, 2, 2-trifluoroethoxy)-2-pyridinyl]methyl]sulphiny1]-</td>
</tr>
<tr>
<td></td>
<td>2-[[[3-methyl-4-(2, 2, 2-trifluoroethoxy)-2-pyridinyl]methyl]sulphiny1]-1H-benzimidazole</td>
</tr>
</tbody>
</table>
Structure

![Chemical Structure Graphic]

Molecular Formula: \( \text{C}_{16}\text{H}_{14}\text{F}_{3}\text{N}_{3}\text{O}_{2}\text{S} \)

Molecular Weight: 369.36

General properties

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.

Description of manufacturing process and process controls

A synthetic flow chart is given in the open part of the DMF.

A signed declaration is given stating that no raw materials of animal origin are used in the manufacturing process.

Characterisation

Evidence of chemical structure has been provided.

Impurities

Details of impurities considered likely from the proposed synthetic route and degradation products have been identified.

Control of active substance

A specification for the active substance has been provided which complies with USP monograph requirements.

There is no BP or Ph.Eur monograph for lansoprazole but a USP monograph exists.

Analytical methods and validation data

Active substance manufacturer

Details of analytical methods and validation of such methods are provided.
**Finished product manufacturer**

The routine tests and methods used by the dosage form manufacturer following receipt of the active raw material have been provided.

**Batch analysis**

The DMF includes batch analytical data for several production batches. Results provided demonstrate compliance with the proposed specification.

**Reference standards or materials**

Certificates of Analysis are provided for lansoprazole reference standard and all named impurity reference standards. They are generally satisfactory.

**Container closure system**

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

**STABILITY**

Overall, the data presented supports the proposed shelf life and storage conditions.

The post approval stability programme is given and is satisfactory.

**DRUG PRODUCT**

**Description and composition of the drug product**

15mg: Hard gelatin capsules, Size 3, white cap marked with ‘L’ and white body marked with ‘15’, containing white to beige gastro-resistant micropellets.

30mg: Hard gelatin capsules, Size 1, white cap marked with ‘L’ and white body marked with ‘30’, containing white to beige gastro-resistant micropellets.
The composition is shown below.

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Reference Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Capsule fill</strong></td>
<td></td>
</tr>
<tr>
<td>Lansoprazole</td>
<td>USP</td>
</tr>
<tr>
<td>Sugar spheres</td>
<td>Ph.Eur</td>
</tr>
<tr>
<td>Sodium starch glycollate (type A)</td>
<td>Ph.Eur</td>
</tr>
<tr>
<td>Sodium lauril sulfate</td>
<td>Ph.Eur</td>
</tr>
<tr>
<td>Povidone K30</td>
<td>Ph.Eur</td>
</tr>
<tr>
<td>Potassium oleate</td>
<td>Ph.Eur</td>
</tr>
<tr>
<td>Hypromellose</td>
<td>Ph.Eur</td>
</tr>
<tr>
<td>Methacrylic acid-ethyl acrylate Co-polymer 1:1 Dispersion 30% (Eudragit L30-D55)</td>
<td>Ph.Eur</td>
</tr>
<tr>
<td>Triethyl citrate</td>
<td>Ph.Eur</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>Ph.Eur</td>
</tr>
<tr>
<td>Talc</td>
<td>Ph.Eur</td>
</tr>
<tr>
<td><strong>Capsules</strong></td>
<td><strong>HSE</strong></td>
</tr>
<tr>
<td><strong>Gelatin shell : Body composition</strong></td>
<td></td>
</tr>
<tr>
<td>Titanium dioxide (E171)</td>
<td>Ph.Eur</td>
</tr>
<tr>
<td>Gelatin</td>
<td>Ph.Eur</td>
</tr>
<tr>
<td><strong>Gelatin shell : Cap composition</strong></td>
<td><strong>HSE</strong></td>
</tr>
<tr>
<td>Titanium dioxide (E171)</td>
<td>Ph.Eur</td>
</tr>
<tr>
<td>Water</td>
<td></td>
</tr>
<tr>
<td>Gelatin</td>
<td>Ph.Eur</td>
</tr>
</tbody>
</table>

The capsules are printed with printing ink that includes the following constituents: Shellac (Lacca), propylene glycol, ammonium hydroxide, potassium hydroxide and black iron oxide.

**Pharmaceutical development**

**Components of the drug product**

The specification for lansoprazole is summarised and is acceptable.

The rationale and function of each excipient added is discussed in this section and in the quality overall expert summary. Excipients used are all well known and are approved for oral products.

**Formulation development**

**Clinical trial formula**

A bioequivalence study has been performed comparing the applicant’s 30mg capsules with the reference product Opiren 30mg capsules. Certificates of Analysis for test and reference products are provided. The formulation for the biobatch is as proposed for marketing. Gastro resistance and dissolution results in buffer conditions are given.
Comparative assay and impurity profile results for three batches of Zoton 15mg Capsules and Opiren 30mg Capsules (biobatch), and two batches each of the applicant’s capsules are provided. The profiles demonstrate essential similarity, as all named and unknown impurities are below the ICH limit for qualification.

Oversages

No overages are required.

Physicochemical and biological properties

The polymorphism of lansoprazole is discussed.

Manufacturing process development

The manufacturing process development is described. Factors considered critical during manufacture are discussed. Process validation studies have been performed with 3 production batches of micro granules which have been used to encapsulate 3 batches each of the 15mg and 30mg capsules.

Container and closure system

Capsules are packaged in HDPE bottles with PP caps (with a desiccant compartment). Formal stability studies have been performed with capsules packaged in the proposed containers.

Microbiological attributes

Capsules comply with Ph.Eur requirements for oral products (Category 3A) at release and throughout the proposed shelf life.

Manufacture

Manufacturer

Batch release and distribution site: Laboratorios Belmac SA, Poligono Industrial Malpica, calle C, Numero 4, 50016 Zaragoza, Spain.

A copy of the manufacturer’s authorisation is provided that covers capsule preparations. A manufacturing certificate issued by the Spanish authorities is also submitted regarding the GMP status of the site.

Batch formula

The manufacturing formula for a maximum production batch size is provided.

Description of manufacturing process and process controls

A satisfactory description of the manufacturing process and process controls is provided.
Process validation and/or evaluation

Process validation data has been provided for the manufacture of three batches of micro granules. The results are satisfactory. Full batch analytical results are also given and show compliance with finished product specification requirements. The process appears to be satisfactorily validated.

An assurance has been given that the encapsulation process will be fully validated up to the maximum batch size proposed.

Control of excipients

Specifications/Analytical procedures/Validation of analytical procedures/Justification of specifications

All excipients in the capsule fill comply with their respective Ph.Eur monographs. The specifications, routine tests and methods performed by the dosage form manufacturer, typical C of A’s from the dosage form manufacturer and supplier are provided and are satisfactory.

Specifications for hard gelatin capsules from the manufacturer are provided and are generally satisfactory. The qualitative and quantitative compositions of the capsule shells, together with specifications are given and are satisfactory. The colouring agent complies with EEC Directive 78/25/EEC and 95/45 requirements.

Confirmation is also given that residual solvents in active and inactive substances are in accordance with guideline requirements.

Excipients of human or animal origin

Oleic acid is of plant origin. Gelatin used in the manufacture of capsules is of bovine origin and is covered by EDQM Certificates of Suitability.

Control of drug product

Specification

Satisfactory specifications for release and shelf life are provided.

Analytical procedures and Validation

Details of analytical procedures and validation data have been supplied.

Batch analysis

Batch analytical data are provided for production scale batches manufactured at the proposed manufacturing site.
Characterisation of impurities

Known impurities are the same as for the active ingredient.

Justification of specifications

The specification proposed is suitably justified and appropriate for this product. Apart from wider limits for assay, the release and shelf life specifications are the same.

Reference standards or materials

Satisfactory details are provided for lansoprazole and impurity reference standards.

Container-closure system

The capsules are packaged in HDPE bottles with a PP cap body (with HDPE cap ring, LDPE cap plug and LDPE container containing a silica gel desiccant). Technical drawings, specifications and routine tests are provided. Suitability for food contact/pharmaceutical use are provided from the suppliers. Typical Certificates of Analysis from the dosage form manufacturer are provided for the bottle and cap.

Stability

Stability summary and conclusion

Stability data are provided for 3 production sized batches of each capsule strength packaged in the proposed HDPE bottle with PP cap, pack size 28 capsules. Samples have been stored at 25°C/60%RH, 30°C/60%RH, and 40°C/75%RH. Testing frequency has been given and is satisfactory.

An in-use stability study has been performed with three batches of the 15mg capsules (pack size 28 caps.). This was considered to represent the highest ratio of free air/volume occupied by capsules inside the container and highest units per container.

Stability data

Overall, the stability data provided supports the proposed shelf life of 24 months and storage conditions (Do not store above 30°C. Store in the original package. Keep the bottle tightly closed to protect from moisture). Although there is no evidence of significant changes at 40°C and the maximum storage temperature of 30°C is strictly not necessary, the applicant wishes to apply the tighter temperature restriction. This is accepted.

Also, based on the results of an in-use stability study, the absence of an in-use stability period is justified.

Post-approval stability protocol and stability commitment

A commitment is given to continue the stability studies in line with the stability protocol.
Lansoprazole is unstable in acidic conditions and is therefore developed as gastroresistant capsules. It exhibits high (80-90%) bioavailability with a single dose. Peak plasma levels occurred within 1.5 to 2.0 hours. As a result, effective acid inhibition is achieved rapidly. 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%. Food reduces its oral bioavailability. 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.

**LAN-2003/006**

Randomized, open-label, cross over study, with two treatment periods of 7 days each, 24 healthy male and female volunteers (23 completed and were analysed) comparing the applicant’s 30mg capsules and reference product Opiren 30mg.

Parametric analysis has been performed using ANOVA and Schuirman tests. Non parametric analysis was by Wilcoxon test and confidence intervals.

Comparative analysis of pharmacokinetic results with Ln transformed variables under fasting conditions are summarised below.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Difference</th>
<th>Difference SE</th>
<th>T/R ratio</th>
<th>90% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ln $C_{\text{max}}$</td>
<td>0.03</td>
<td>0.11</td>
<td>96.79</td>
<td>80.13-116.92%</td>
</tr>
<tr>
<td>Ln AUC$_{\text{inf}}$</td>
<td>0.02</td>
<td>0.08</td>
<td>102.33</td>
<td>89.57-116.91%</td>
</tr>
<tr>
<td>Ln AUC$_{\text{last}}$</td>
<td>0.03</td>
<td>0.08</td>
<td>102.54</td>
<td>88.96-118.20%</td>
</tr>
<tr>
<td>Ln $C_{\text{max}}$/AUC$_{\text{last}}$</td>
<td>-0.06</td>
<td>0.04</td>
<td>94.39</td>
<td>87.77-101.52</td>
</tr>
</tbody>
</table>

Wilcoxon test (variable: $T_{\text{max}}$).

<table>
<thead>
<tr>
<th>Statistical significance (p bilateral)</th>
<th>Median of difference (hrs)</th>
<th>CI 90% difference (hrs)</th>
<th>CI 90% difference with respect to reference average</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1688</td>
<td>0.12</td>
<td>0 to 0.5</td>
<td>100-127.23%</td>
</tr>
</tbody>
</table>

Comparative analysis of pharmacokinetic results with Ln transformed variables under fed conditions are summarised below.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Difference</th>
<th>Difference SE</th>
<th>T/R ratio</th>
<th>90% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ln $C_{\text{max}}$</td>
<td>0.19</td>
<td>0.10</td>
<td>82.34</td>
<td>69.8 –97.03%</td>
</tr>
<tr>
<td>Ln AUC$_{\text{inf}}$</td>
<td>0.03</td>
<td>0.07</td>
<td>102.83</td>
<td>91.83-115.14%</td>
</tr>
<tr>
<td>Ln AUC$_{\text{last}}$</td>
<td>0.05</td>
<td>0.06</td>
<td>94.84</td>
<td>86.16-104.39%</td>
</tr>
<tr>
<td>Ln $C_{\text{max}}$/AUC$_{\text{last}}$</td>
<td>-0.14</td>
<td>0.06</td>
<td>86.82</td>
<td>78.04-96.58%</td>
</tr>
</tbody>
</table>

Wilcoxon test (variable: $T_{\text{max}}$).

<table>
<thead>
<tr>
<th>Statistical significance (p bilateral)</th>
<th>Median of difference (hrs)</th>
<th>CI 90% difference (hrs)</th>
<th>CI 90% difference with respect to reference average</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.0001</td>
<td>1.375</td>
<td>0.83 - 1.665</td>
<td>126.54-153.25%</td>
</tr>
</tbody>
</table>
The 90% CI for AUC₀-t, AUC₀-inf and Cₘₐₓ ratios are within the normally acceptable range for bioequivalence (80-125%). The two products (applicant’s 30mg versus Opiren 30mg capsules) are considered bioequivalent when taken under fasting conditions.

In the fed study, the 90% CI for AUC₀-t and AUC₀-inf ratios were within the normally acceptable range for bioequivalence (80-125%). A wider 90% CI acceptance criteria for Cₘₐₓ (70-143%) was proposed in the protocol as a result of the well known pharmacokinetic variability of lansoprazole and the less clinical relevance for this parameter in bioequivalence determination. The lower 90% CI for Cₘₐₓ is outside the wider limits of 70-143% (see Clinical Assessment).

Dissolution results for UK Zoton capsules are similar to that for the reference product and therefore results are also applicable to UK Zoton 30mg capsules.

A bio-equivalence study of the 15mg strength has not been performed and this has been suitably justified in the expert report.

**RECOMMENDATION**

Marketing Authorisations should be granted.
PRECLINICAL ASSESSMENT

No new preclinical data have been supplied with this application and none are required.
CLINICAL ASSESSMENT

PRODUCT LICENCE NOs: PL 08608/0066-71
PRODUCT NAMES: Lansoprazole 15mg Gastro-resistant Capsules
                  Lansoprazole 30mg Gastro-resistant Capsules
ACTIVE (S): Lansoprazole
COMPANY NAME: Olinka UK Ltd
LEGAL STATUS: POM

INTRODUCTION AND BACKGROUND

These are one complex and 5 standard abridged national marketing authorisation applications for Lansoprazole 15mg and 30mg Capsules (3 pairs of applications) made under Directive 2001/83/EC Article 10.1(a)(iii), first paragraph. The proposed legal status is POM.

Lansoprazole belongs to 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.

The reference medicinal products are Zoton 15mg and 30 mg capsules (PLs 00011/0287-8 John Wyeth & Brother [originally PL 00095/0264-5 Cyanamid of Great Britain Ltd]). The originator product in the EU [France] is Ogast 30mg Gelule [Laboratoire Takeda] – first authorised November 1990.

INDICATIONS

The indications are in line with the reference product’s SPC, except that all references to the use of lansoprazole with antibiotics in the treatment of H. pylori infection have been omitted at the request of the applicant. Although it is clinically undesirable not to have harmonised SPCs for lansoprazole, the applicant has provided legally sound arguments based on Article 11 of Directive 2004/27/EC (amending Directive 2001/83/EC).

DOSE & DOSE SCHEDULE

The dose and dosage schedule are in line with the SPC for the reference product, except that reference to the eradication of H. pylori infection has been omitted.

CLINICAL PHARMACOLOGY

Pharmacodynamic properties

Lansoprazole is a proton pump inhibitor, inhibiting 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, wherein 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.

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

**Bioequivalence**

**Study**


**Design**

Randomised, open label, cross-over – separated by a 7-day wash out. 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

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Values</th>
<th>Ratio</th>
<th>90% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean +/- SD (range)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Opiren</strong></td>
<td></td>
<td>Belmac lansoprazole</td>
<td></td>
</tr>
<tr>
<td>AUClast (ng.h/ml)</td>
<td>3299.0 +/- 2451.4 (513.5 – 10458.6)</td>
<td>3330.1 +/- 2458.7 (852.8 – 10303.0)</td>
<td>102.54</td>
</tr>
<tr>
<td>AUCinf (ng.h/ml)</td>
<td>3483.9 +/- 2877.7 (587.0 – 12004.4)</td>
<td>3525.2 +/- 2904.1 (863.8 – 12264.2)</td>
<td>102.33</td>
</tr>
<tr>
<td>Cmax (ng/ml)</td>
<td>1080.4 +/- 482.0 (132.5 – 2300.7)</td>
<td>1035.4 +/- 464.5 (158.5 – 2151.9)</td>
<td>96.79</td>
</tr>
<tr>
<td>Tmax(h)</td>
<td>1.84 +/- 0.66 (1.00 – 3.97)</td>
<td>2.32 +/- 1.19 (1.00 – 6.00)</td>
<td>-</td>
</tr>
</tbody>
</table>
Summary of main pharmacokinetic parameters of lansoprazole (Fed) - N=24

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Values</th>
<th>Ratio</th>
<th>90% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opiren</td>
<td>Belmac lansoprazole</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUClast (ng.h/ml)</td>
<td>3098.6 +/- 1788.7 (907.4 – 8783.3)</td>
<td>94.84</td>
<td>86.16 to 104.39</td>
</tr>
<tr>
<td>AUCinf (ng.h/ml)</td>
<td>3299.2 +/- 2229.0 (725.8 – 11247.4)</td>
<td>102.83</td>
<td>91.83 to 115.4</td>
</tr>
<tr>
<td>Cmax (ng/ml)</td>
<td>892.1 +/- 367.1 (298.6 – 1944.3)</td>
<td>82.34</td>
<td>69.87 to 97.03</td>
</tr>
<tr>
<td>Tmax (h)</td>
<td>3.13 +/- 1.15 (1.67 – 6.00)</td>
<td>-</td>
<td>-</td>
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</tbody>
</table>

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 15mg and 60mg range. The reference product is stated to be identical to the UK reference product.

Under non-fasting conditions, the AUC parameters were supportive for bioequivalence of the test and reference products. The $C_{\text{max}}$ 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.

Efficacy

An overview of the efficacy and safety of lansoprazole was provided, which is satisfactory. Lansoprazole has been licensed worldwide for over 10 years.

SUMMARY OF PRODUCT CHARACTERISTICS (SPC) PATIENT INFORMATION LEAFLET LABELLING

Satisfactory.

Discussion

The products are considered to be within the acceptable bioequivalence range as the reference products and the product literature is clinically satisfactory.

Recommendation

There are no clinical reasons not to grant marketing authorisations for these two strengths of lansoprazole.
OVERALL CONCLUSION AND RISK-BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of Lansoprazole 15mg 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 Capsules and Zoton Capsules (PLs 00011/0287-8).

No new or unexpected safety concerns arise from these applications.

The SPC, PIL and labelling are satisfactory and consistent with those of Zoton 15mg and 30mg Capsules.

RISK-BENEFIT ASSESSMENT

The quality of the products 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 assessment is therefore considered to be favourable.
**LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES**
**PL 08608/0066, 0068, 0070**

**LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES**
**PL 08608/0067, 0069, 0071**

**STEPS TAKEN FOR ASSESSMENT**

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<table>
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<tbody>
<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation applications for Lansoprazole 15mg Capsules / Lansoprazole 30mg Capsules on 17 February 2004.</td>
</tr>
<tr>
<td>2</td>
<td>The MHRA’s assessment of the submitted quality data was completed on 22 September 2004.</td>
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<td>3</td>
<td>Further information (quality) was requested from the company on 1 October 2004.</td>
</tr>
<tr>
<td>4</td>
<td>The MHRA’s assessment of the submitted clinical data was completed in December 2004 and revised in February 2005.</td>
</tr>
<tr>
<td>5</td>
<td>The applicant’s responses to further information (quality) request were sent in letters dated 24 March 2005 and 15 August 2005.</td>
</tr>
<tr>
<td>6</td>
<td>The applicant requested changes to the product particulars (SPC and PIL) in September 2005.</td>
</tr>
<tr>
<td>7</td>
<td>Further information (quality) was requested from the company on 8 November 2005.</td>
</tr>
<tr>
<td>8</td>
<td>The applicant’s response to further information (quality) request was received on 17 November 2005.</td>
</tr>
<tr>
<td>9</td>
<td>The licence was granted with effect from 9 December 2005.</td>
</tr>
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</table>
LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 08608/0066, 0068, 0070

LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0067, 0069, 0071

STEPS TAKEN AFTER AUTHORISATION - SUMMARY

<table>
<thead>
<tr>
<th>Date submitted</th>
<th>Application type</th>
<th>Scope</th>
<th>Outcome</th>
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</table>
SUMMARY OF PRODUCT CHARACTERISTICS

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 gastrointestinal 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.

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

ATC Code: A02B C03

Lansoprazole is a member of a class of drugs called proton pump inhibitors. Its mode of action is to inhibit specifically the H+/K+ ATPase (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
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.

5.3 Preclinical safety data

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

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

**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 30°C. 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 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 08608/0066
9 DATE OF FIRST AUTHORIZATION/RENEWAL OF THE AUTHORISATION

09/12/2005

10 DATE OF REVISION OF THE TEXT

09/12/2005
SUMMARY OF PRODUCT CHARACTERISTICS

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 gastrointestinal 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.

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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).

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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

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

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

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

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

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

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

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

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

Dermatological reactions include skin rashes, urticaria and pruritus. These generally resolve on discontinuation of drug therapy. Serious dermatological reactions are rare but there have been occasional reports of Stevens-Johnson Syndrome, toxic epidermal necrolysis and erythematous or bullous rashes including erythema multiforme. Cases of hair thinning and photosensitivity have also been reported.
Other hypersensitivity reactions include angioedema, wheezing, and very rarely, anaphylaxis. Cases of interstitial nephritis have been reported which have sometimes resulted in renal failure.

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

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

Gynaecomastia and impotence have been reported rarely.

4.9 Overdose

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code A02B C03

Lansoprazole is a member of a class of drugs called proton pump inhibitors. Its mode of action is to inhibit specifically the H+ / K+ ATPase (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

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.

5.3 Preclinical safety data

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

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

**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 integral silica gel desiccant.

Packs of 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 08608/0067
DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
09/12/2005

DATE OF REVISION OF THE TEXT
09/12/2005
SUMMARY OF PRODUCT CHARACTERISTICS

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 gastrointestinal 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.

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

ATC Code: A02B C03

Lansoprazole is a member of a class of drugs called proton pump inhibitors. Its mode of action is to inhibit specifically the H+ / K+ ATPase (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 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
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.

5.3 Preclinical safety data

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

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

**Capsule Content:**
Sugar spheres (sucrose and maize starch)
Sodium starch glycolate Type A
Sodium laurilsulfate
Povidone K30
Potassium oleate
Oleic acid
Hypermellose
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 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 08608/0068
9  DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

09/12/2005

10  DATE OF REVISION OF THE TEXT

09/12/2005
SUMMARY OF PRODUCT CHARACTERISTICS

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 gastrointestinal 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

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

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

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

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

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

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

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

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

Dermatological reactions include skin rashes, urticaria and pruritus. These generally resolve on discontinuation of drug therapy. Serious dermatological reactions are rare but there have been occasional reports of Stevens-Johnson Syndrome, toxic epidermal necrolysis and erythematous or bullous rashes including erythema multiforme. Cases of hair thinning and photosensitivity have also been reported.
Other hypersensitivity reactions include angioedema, wheezing, and very rarely, anaphylaxis. Cases of interstitial nephritis have been reported which have sometimes resulted in renal failure.

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

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

Gynaecomastia and impotence have been reported rarely.

4.9 Overdose

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code A02B C03

Lansoprazole is a member of a class of drugs called proton pump inhibitors. Its mode of action is to inhibit specifically the H+ / K+ ATPase (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

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.

5.3 Preclinical safety data

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

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

**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 30°C. 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 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 08608/0069
9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

09/12/2005

10 DATE OF REVISION OF THE TEXT

09/12/2005
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 gastrointestinal 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.

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.
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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

ATC Code: A02B C03

Lansoprazole is a member of a class of drugs called proton pump inhibitors. Its mode of action is to inhibit specifically the H+ / K+ ATPase (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 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

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.

5.3 Preclinical safety data

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

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

**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 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 08608/0070
9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

09/12/2005

10 DATE OF REVISION OF THE TEXT

09/12/2005
SUMMARY OF PRODUCT CHARACTERISTICS

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 gastrointestinal 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

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

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

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

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

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

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

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

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

Dermatological reactions include skin rashes, urticaria and pruritus. These generally resolve on discontinuation of drug therapy. Serious dermatological reactions are rare but there have been occasional reports of Stevens-Johnson Syndrome, toxic epidermal necrolysis and erythematous or bullous rashes including erythema multiforme. Cases of hair thinning and photosensitivity have also been reported.
Other hypersensitivity reactions include angioedema, wheezing, and very rarely, anaphylaxis. Cases of interstitial nephritis have been reported which have sometimes resulted in renal failure.

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

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

4.9 Overdose

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC Code A02B C03

Lansoprazole is a member of a class of drugs called proton pump inhibitors. Its mode of action is to inhibit specifically the H+ / K+ ATPase (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

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.

5.3 Preclinical safety data

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

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

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

**Capsule content:**
Sugar spheres (sucrose and maize starch)
Sodium starch glycolate Type A
Sodium lauril sulfate
Povidone K30
Potassium oleate
Oleic acid
Hypermellose
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 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 08608/0071
9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

09/12/2005

10 DATE OF REVISION OF THE TEXT

09/12/2005
Patient Information Leaflet

LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 08608/0066, 0068, 0070

LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0067, 0069, 0071
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:
1. What Lansoprazole Capsules are and what they are used for
2. Before you take Lansoprazole Capsules
3. How to take Lansoprazole Capsules
4. Possible side effects
5. Storing Lansoprazole Capsules

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 lauryl sulphate, povidone, potassom 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 (biscuit), propylene glycol, ammonium hydroxide, potassium hydroxide, black iron oxide (E172).

Lansoprazole 15 mg Capsules are supplied in bottles of 28 or 56 capsules (2x bottles of 28 capsules).*
Lansoprazole 30 mg Capsules are supplied in bottles of 28 or 56 capsules (2x bottles of 28 capsules).*
(* Only the marketed pack sizes will be stated on the printed leaflet.

Lansoprazole Capsules are manufactured by Laboratorios Belmex SA, Poligono Industrial Malbica, calle C, 50016 Zaragoza, Spain.

Marketing Authorisation Holder
Olnika UK Limited, 3840 Chamborley Rd, London NW10 6JE, United Kingdom.

Distributed by:
Arrow Genetics Limited, Unit 2, Eastman Way, Stevenage, Hertfordshire SG1 4SZ, 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. It is given to:
- heal ulcers in your stomach or duodenum, including ulcers that are caused by other medicines called Non-Steroidal Anti-Inflammatory Drugs (also known as 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 above.

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
Inform your doctor if you are pregnant, planning to become pregnant or you are breastfeeding. Your doctor will decide if you should take Lansoprazole Capsules.

Driving and using machines:
There should be no effect on your 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 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
Lansoprazole 15mg/30mg Gastro-resistant Capsules PL 08608/0066-71

It's 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.

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 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. This is a very serious but rare side effect. You may need urgent medical attention or hospitalisation.
- 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 and unexpected bruising or bleeding.

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

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

Swollen lips and swelling of the mouth. Soreness of the mouth and throat, or a dry mouth, also might occur.

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.

Side effects also include sensitivity to light and hair loss.

There have been rare reports of joint and muscle pain, swelling of limbs, blurred vision, large breasts, impotence, blood disorders, taste disorders, kidney or liver problems, pins and needles, and numbness.

Very rarely, you may feel sleepy, confused, nervous, depressed or you may hallucinate.

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).

Tell your doctor if you 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 December 2005.
PATIENT INFORMATION LEAFLET

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

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

In this leaflet:
1. What Lansoprazole Capsules are and what they are used for
2. Before you take Lansoprazole Capsules
3. How to take Lansoprazole Capsules
4. Possible side effects
5. Storing Lansoprazole Capsules

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 1 and white body marked with 15 or 30, which 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 laurylsulphate, povidone, potassium oleate, steric acid, hypromellose, methacrylic acid - ethyl acrylate copolymer 1:1, tridihyl citrate, titanium dioxide (E171), talc and gelatin. The printing ink on the capsules contains the following additional ingredients: shellac (laccsa), propylene glycol, ammonium hydrogen phosphate, potassium hydrogen phosphate, black iron oxide (E172).

Lansoprazole 15 mg Capsules are supplied in bottles of 28 or 56 capsules (2 x bottles of 28 capsules). *
Lansoprazole 30 mg Capsules are supplied in bottles of 28 or 56 capsules (2 x bottles of 28 capsules). *

(‘*’ on the marketing pack sizes will be stated on the printed literature)

Lansoprazole Capsules are manufactured by Laboratorios Beltrac SA, Poligono Industrial Malpica, calle C, 50016 Zaragoza, Spain

Marketing Authorisation Holder

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 help your condition, as it is very good at reducing the amount of acid your stomach makes. It is given to:

• 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.
• 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 above.

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
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 or 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 may 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 chemical 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's 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.

There is no experience of this product in children.

**HEALING OF STOMACH ULCERS**
Take one 30 mg capsule every day for 4 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-ESOPHAGEAL REFUX 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 DYSPESIA**
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 or 30 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.

**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 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. This is a very serious but rare side effect. You may need urgent medical attention or hospitalisation.
- Collitis (persistent and severe diarrhoea leading to significant weight loss), jaundice (yellowing of the skin or whites of the eyes), severe redness and blistering of the skin and unexpected bruising or bleeding.

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

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

Swollen lips and swelling of the mouth.

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

Side effects also include sensitivity to light and hair loss.

There have been rare reports of joint and muscle pain, swelling limbs, blurred vision, larger breasts, impotence, blood disorders, taste disorders, kidney or liver problems, pins and needles and, numbness.
Patient Information Leaflet

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

In this leaflet:
1. What Lansoprazole Capsules are and what they are used for
2. Before you take Lansoprazole Capsules
3. How to take Lansoprazole Capsules
4. Possible side effects
5. Storing Lansoprazole Capsules

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 lauryl sulphate, 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 (lacc), propylene glycol, ammonium hydroxide, potassium hydroxide, and black iron oxide (E172).
Lansoprazole 15 mg Capsules are supplied in bottles of 28 or 56 capsules (2 x bottles of 28 capsules),
Lansoprazole 30 mg Capsules are supplied in bottles of 28 or 56 capsules (2 x bottles of 28 capsules).

(Only the marketed pack sizes will be stated on the printed leaflet.)
Lansoprazole Capsules are manufactured by Laboratorios Belmeq SA, Pellegrino Industrial Malpica, calle C, 50016 Zaragoza, Spain

Marketing Authorisation Holder
Olinta (UK) Limited, 3849 Chamberlayne Rd., London NW10 3JE, United Kingdom.

Distributed by
PLIVA Pharma Ltd, Vision House, Bedford Road, Petersfield, Hampshire, GU32 3QB, UK

1. WHAT LAN SOPRAZOLE 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. It is given to:
• 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.
• 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 LAN SOPRAZOLE 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 above.
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
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
• phenytion 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’s 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.

There is no experience of this product in children.

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 ZOLLLINGER-ELLISON SYNDROME
Take two 30 mg capsules every day. Then, depending on how you respond, your doctor may change your dose.

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 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. This is a very serious but rare side effect. You may need urgent medical attention or hospitalisation.
- 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 and unexpected bruising or bleeding.
- The most common side effects are headache, dizziness, tiredness and generally feeling unwell.
- Other side-effects sometimes seen are stomach upsets including diarrhoea or constipation, feeling or being sick, wind and stomach ache.
- Swollen lips and swelling of the mouth.
- Soreness of the mouth and throat, or a dry mouth, also might occur.
- Skin reactions including skin blistering, urticaria (characterised by large red wheals in the skin) and pruritus (itching) can occur. Rarely, much more severe skin reactions occur; these affect large areas of the skin associated with redness, rash, blistering and peeling.
- Side effects also include sensitivity to light and hair loss.
- There have been rare reports of joint and muscle pain, swollen limbs, blurred vision, larger breasts, impotence, blood disorders, taste disorders, kidney or liver problems, pins and needles and, numbness.
- Very rarely, you may feel sleepy, confused, nervous, depressed or you may hallucinate.
- 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).
- Tell your doctor if you 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 December 2005
Lansoprazole 15mg & 30mg Gastro-Resistant Capsules

Patient Information Leaflet

Read all of this leaflet carefully before you start taking this medicine
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- This medicine has been prescribed for you personally and you should not pass it on to others. It may harm them, even if their symptoms are the same as yours.

In this leaflet
1. What Lansoprazole Capsules are and what they are used for
2. Before you take Lansoprazole Capsules
3. How to take Lansoprazole Capsules
4. Possible side effects
5. Storing Lansoprazole Capsules

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 (saccharine and maize starch), sodium starch glycolate, sodium lauryl sulphate, povidone, potassium oleate, citric acid, hypromellose, methacrylic acid - ethyl acrylate copolymer 1:1, methyl cellulose, titanium dioxide (E172), talc and gelatin.
- The printing ink on the capsules contains the following additional ingredients: black (titanium dioxide, ferric oxide (E 172).

Lansoprazole 15 mg Capsules are supplied in bottles of 28 or 56 capsules (2 x bottles of 28 capsules).
Lansoprazole 30 mg Capsules are supplied in bottles of 28 or 56 capsules (2 x bottles of 28 capsules).
(only the marketed pack sizes will be stated on the printed labels)

Lansoprazole Capsules are manufactured by Laboratorios Belmec SA, Poligono Industrial Milpica, calle C, 01016 Zaragoza, Spain.

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

Distributed by
Radarchem Limited, 27 Old Gloucester Street, London WC1 3XX, 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. It is given to:
- 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.
- 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 above.

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
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 patient information leaflet 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's 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.

There is no experience of this product in children.

**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 NSAI**
Take one 15 mg or 30 mg capsule every day for as long as your doctor prescribes.

**GASTRO-OESOPHAGEAL REFUX 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 DYSPESPIA**
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 NSAI**
Take one 15 mg or 30 mg capsule every day for 4 to 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 ZOLLLINGER-ELLISON SYNDROME**
Take two 30 mg capsules every day. Then, depending on how you respond, your doctor may change your dose.

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 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 (inflammation): e.g. swelling of the face, lips, tongue or throat, or difficulty breathing or swallowing. This is a very serious but rare side effect. You may need urgent medical attention or hospitalisation.
  - 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 and unexpected bruising or bleeding.
  - The most common side effects are headache, dizziness, tiredness and generally feeling unwell.

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

Swollen lips and swelling of the mouth.

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

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

Side effects also include sensitivity to light and hair loss.

There have been rare reports of joint and muscle pain, swollen limbs, blurred vision, larger breasts, impotence, blood disorders, taste disorders, kidney or liver problems, pins and needles and, numbness.

Very rarely, you may feel sleepy, confused, nervous, depressed or you may hallucinate.

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).

Tell your doctor if you 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 December 2005.
Labels/Packaging
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 15MG GASTRO-RESISTANT CAPSULES
PL 08608/0066
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 exceed 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 sodium. Refer to leaflet for further information.
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 15MG GASTRO-RESISTANT CAPSULES
PL 08608/0066

Lansoprazole 15mg Gastro-Resistant Capsules

Each capsule contains 15mg lansoprazole. Also contains sucrose. Refer to leaflet for further information.

MHRA: PAR – Lansoprazole 15mg/30mg Gastro-resistant Capsules PL 08608/0066-71
LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 08608/0066
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 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0067

Lansoprazole 30 mg Gastro-Resistant Capsules
Keep out of the reach and sight of children.

For oral use only. Take as directed by your doctor. Do no store above 30°C.
Store in the original package. Keep the packet tightly closed to protect from moisture.

Distributor: Aventis Generics Ltd, Steventon, RG7 4SH, PL 08608/0067
MA number: CT/2013/103, 39/40 Charnley Street, London NW1 3LT,

Tamaño real 18 x 110 mm

PANTONE Blue 072
PANTONE 355
NEGRO
LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0067
LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0067

Tamaño real 18 x 110 mm

PANTONE Blue 072
NEGRO
LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0067
LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0067

For oral use only.
Swallow the capsule 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.
Tamaño real 18 x 110 mm

NEGRO
PANTONE Purple
PANTONE Green
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 booklet 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.

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.

POM
PL 08608/0068

AM (holder):
Otsuka (UK) Limited,
3840 Chiswick High Road,
London NW10 0JR
United Kingdom.

Distributed by:
Arrow Bemutók Limited,
Unit 2, Eastman Way, Stevenage,
Hertfordshire, SG1 4SZ
United Kingdom.
LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 08608/0068

Translation of Braille on outer cartons:
Braille text reads as follows:

=lans-
oprazole
#15mg
capsules

Note:
# = number sign
* = letter sign

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:
Lansoprazole 15 mg
Each bottle contains:
56 gastro-resistant capsules

Lansoprazole 15 mg Gastro-Resistant Capsules
50 capsules (2 x bottles of 25 capsules)
LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 08608/0068
LAN SOPRA ZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 08608/0068

Tamaño real 13 x 100 mm

PANTONE 288
PANTONE 326
LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 08608/0068

Tamaño real 13 x 100 mm

- NEGRO
- PANTONE Process Magenta
- PANTONE Green
LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0069

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 25°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.

MHRA: PAR – Lansoprazole 15mg/30mg Gastro-resistant Capsules PL 08608/0066-71

117
LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0069

Tamaño real 18 x 110 mm

PANTONE Blue 072
PANTONE 355
NEGRO
LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0069
LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0069
LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0069

PANTONE 288
PANTONE Rubine Red
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 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0069

Tamaño real 18 x 110 mm

- NEGRO
- PANTONE Purple
- PANTONE Green
LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 08608/0070
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 packaging. Keep the container tightly closed to protect from moisture.

Please read the enclosed leaflet before use. KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.

For 15mg dosage:

Lansoprazole 15mg Gastro-Resistant Capsules

Each capsule contains 15mg lansoprazole. Also contains sucrose. Refer to leaflet for further information.
LANSOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 08608/0070
LAN SOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 08608/0070
LAN SOPRAZOLE 15MG GASTRO-RESISTANT CAPSULES
PL 08608/0070
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
28 capsules

Each gastro-resistant capsule contains
30 mg lansoprazole. Also contains sucrose.
Refer to leaflet for further information.

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.

Distributed by Arrow Generics Limited,
Unit 2, Eastman Way, Stevenage,
Hertfordshire, SG1 4SZ
United Kingdom.

MA Holder:
Gliveca UK Limited,
3B/40 Chamberlayne Road,
London NW10 3JL
United Kingdom.

PL 08608/0071

MHRA: PAR – Lansoprazole 15mg/30mg Gastro-resistant Capsules PL 08608/0066-71
LANSOPRAZOLE 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0071
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PL 08608/0071

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 30MG GASTRO-RESISTANT CAPSULES
PL 08608/0071

Each capsule contains 30mg of lansoprazole. Also contains ascorbic acid, microcrystalline cellulose, magnesium stearate, sodium lauryl sulphate, sodium starch glycolate, titanium dioxide and vanillin.

Tamaño real 18 x 110 mm

NEGRO
PANTONE Purple
PANTONE Green