LANSOPRAZOLE 15 MG GASTRO-RESISTANT CAPSULES
LANSOPRAZOLE 30 MG GASTRO-RESISTANT CASPSULES

PL 14017/0183-6

UKPAR

TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lay Summary</td>
<td>2</td>
</tr>
<tr>
<td>Scientific discussion</td>
<td>3</td>
</tr>
<tr>
<td>Steps taken for assessment</td>
<td>13</td>
</tr>
<tr>
<td>Summary of Product Characteristics</td>
<td>14</td>
</tr>
<tr>
<td>Product Information Leaflet</td>
<td>29</td>
</tr>
<tr>
<td>Labelling</td>
<td>37</td>
</tr>
</tbody>
</table>
LAY SUMMARY

The MHRA granted Dexcel Pharma Limited Marketing Authorisations (licences) for the medicinal products Lansoprazole 15 mg and 30 mg Gastro-Resistant Capsules (PL 14017/0183-6) on 24 November 2010. These products are prescription-only medicines (POM).

Lansoprazole 15 mg and 30 mg Gastro-Resistant Capsules are used for the following indications:

- Treatment of duodenal and stomach ulcer
- Treatment of inflammation in your oesophagus (reflux oesophagitis)
- Prevention of reflux oesophagitis
- Treatment of heartburn and acid regurgitation
- Treatment or prevention of duodenal or stomach ulcer in patients requiring continued Non-Steroidal Anti-Inflammatory Drug (NSAID) treatment (NSAID treatment is used against pain or inflammation)
- Treatment of Zollinger-Ellison syndrome

The active ingredient lansoprazole is a proton pump inhibitor. Proton pump inhibitors reduce the amount of acid that your stomach makes.

No new or unexpected safety concerns arose from these applications and it was, therefore, judged that the benefits of taking Lansoprazole 15 mg and 30 mg Gastro-Resistant Capsules outweigh the risks, hence Marketing Authorisations have been granted.
LANSOPRAZOLE 15 MG GASTRO-RESISTANT CAPSULES
LANSOPRAZOLE 30 MG GASTRO-RESISTANT CAPSULES
PL 14017/0183-6

SCIENTIFIC DISCUSSION

TABLE OF CONTENTS

Introduction Page 4
Pharmaceutical assessment Page 5
Non-clinical assessment Page 8
Clinical assessment Page 9
Overall conclusions and risk benefit assessment Page 12
INTRODUCTION

The UK granted Marketing Authorisations for the medicinal products Lansoprazole 15 mg and 30 mg Gastro-Resistant Capsules (PL 14017/0183-6) to Dexcel Pharma Limited on 24 November 2010. These products are available as prescription-only medicines (POM) and are indicated for the:

- Treatment of duodenal and gastric ulcer
- Treatment of reflux oesophagitis
- Prophylaxis of reflux oesophagitis
- Treatment of NSAID-associated benign gastric and duodenal ulcers in patients requiring continued NSAID treatment
- Prophylaxis of NSAID-associated gastric ulcers and duodenal ulcers in patients at risk (see section 4.2) requiring continued therapy
- Symptomatic gastroesophageal reflux disease
- Zollinger-Ellison syndrome.

Lansoprazole is a gastric proton pump inhibitor. It inhibits the final stage of gastric acid formation by inhibiting the activity of H⁺/K⁺ ATPase of the parietal cells in the stomach. The inhibition is dose-dependent and reversible, and the effect applies to both basal and stimulated secretion of gastric acid. Lansoprazole is concentrated in the parietal cells and becomes active in their acidic environment, whereupon it reacts with the sulphydryl group of H⁺/K⁺ ATPase causing inhibition of the enzyme activity.

The applications were submitted under Article 10(1) of Directive 2001/83/EC, as amended. The proposed products are generic medicinal products of Ogast 15 mg and 30 mg Capsules), which were first authorised in France to Takeda in December 1991. The reference medicinal products in the UK are Zoton 15 mg and 30 mg Capsules (PL 00095/0302 and 0264), which were authorised to Cyanamid of Great Britain Ltd in January 1996.

No new non-clinical studies were performed, which is acceptable given that the proposed products are generic medicinal products of originator products that have been licensed for over 10 years.

Two single-dose, bioequivalence studies under fasting and fed conditions using the lansoprazole 30mg strength capsule were submitted to support the applications. The bioequivalence studies were carried out in accordance with Good Clinical Practice (GCP).

With the exception of the bioequivalence studies, no new clinical studies were performed, which is acceptable given that the proposed products are generic medicinal products of originator products that have been licensed for over 10 years.

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

ACTIVE SUBSTANCE
INN: Lansoprazole
Chemical Name: 2-[[3-methyl-4-(2,2,2-trifluoroethoxy)-2-pyridinyl]methyl]sulfinyl]-1H-benzimidazole
Molecular Formula: C_{16}H_{14}F_{3}N_{3}O_{2}S
Structure:

![Molecular Structure Image]

Molecular weight: 369.3
Appearance: A white to off white powder, practically insoluble in water, soluble in anhydrous ethanol and very slightly soluble in acetonitrile. The substance exhibits polymorphism.

Lansoprazole is the subject of a European Pharmacopoeia monograph.

All aspects of the manufacture and control of the active substance lansoprazole are covered by a European Directorate for the Quality of Medicines (EDQM) Certificate of Suitability.

MEDICINAL PRODUCT
Other ingredients
All capsule strengths contain the pharmaceutical excipients sugar spheres (sucrose and maize starch), sodium laurilsulfate, meglumine, mannitol (E421), hypromellose, macrogol 6000, talc, polysorbate 80, gelatin, titanium dioxide (E171) and methacrylic acid-ethyl acrylate copolymer (1:1), dispersion 30%. In addition, the 15 mg strength also contains quinoline yellow (E104) in the capsule shell.

All excipients comply with their respective European Pharmacopoeia monograph. Suitable batch analysis data have been provided for each excipient, showing compliance with their respective monograph/specification.

With the exception of gelatin, none of the other excipients contain materials of animal or human origin. The supplier of gelatin has provided a European Directorate for the Quality of Medicines (EDQM) Certificate of Suitability to show that its production is consistent with current regulations concerning the minimising of transmission of BSE/TSE. No
genetically modified organisms (GMO) have been used in the preparation of these products.

**Pharmaceutical Development**

The objective of the development programme was to produce safe, efficacious products containing 15 mg and 30 mg lansoprazole that could be considered generic medicinal products of Zoton 15 mg and 30 mg Capsules (Cyanamid of Great Britain Ltd, UK).

A satisfactory account of the pharmaceutical development has been provided.

Comparative *in vitro* dissolution and impurity profiles have been provided for the proposed and originator products.

**Manufacturing Process**

A description and flow-chart of the manufacturing method have been provided. In-process controls are satisfactory based on process validation data and controls on the finished product. Process validation on batches of each strength has been provided.

**Finished product specification**

The finished product specifications are satisfactory. Test methods have been described and have been adequately validated. Batch data have been provided and comply with the release specifications. Certificates of analysis have been provided for all working standards used.

**Container Closure System**

All strengths of the capsule are packaged in aluminium/aluminium blister strips in pack sizes of 28 capsules.

Satisfactory specifications and certificates of analysis have been provided for all packaging components. All primary packaging complies with the current European regulations concerning materials suitable for contact with food.

**Stability of the Product**

Stability studies were performed in accordance with current guidelines on batches of finished product packed in the packaging proposed for marketing. The data from these studies support a shelf-life of 2 years, with the special storage conditions ‘Do not store above 25ºC. Store in the original package in order to protect from moisture.’

**Bioequivalence/Bioavailability**

Satisfactory certificates of analysis have been provided for the test and reference batches used in the bioequivalence studies.

**Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and Labelling**

The SmPCs, PIL and labelling are pharmaceutically satisfactory.

**MAA Forms**

The MAA forms are satisfactory.
Expert Report
The pharmaceutical expert report is written by an appropriately qualified person and is a suitable summary of the pharmaceutical aspects of the dossier.

Conclusion
The grant of Marketing Authorisations is recommended.
NON-CLINICAL ASSESSMENT

PHARMACODYNAMICS, PHARMACOKINETICS AND TOXICOLOGY
No new non-clinical studies were performed, which is acceptable given that the proposed products are generic medicinal products of originator products that have been licensed for over 10 years.

NON-CLINICAL EXPERT REPORT
The non-clinical expert report has been written by an appropriately qualified person and is satisfactory, providing an appropriate review of the non-clinical aspects of the dossier.

ENVIRONMENTAL RISK ASSESSMENT
An environmental risk assessment was not submitted and none is required for these applications. This is acceptable given that these products are intended for generic substitution with the market leaders and, as such, will be used instead of not additional to other such products on the market (thus not increasing any environmental impact).

CONCLUSION
The grant of Marketing Authorisations is recommended.
CLINICAL ASSESSMENT

PHARMACOKINETICS
In support of these applications, the marketing authorisation holder has submitted the following two bioequivalence studies:

Study 1
A randomised, open-label, single-dose, two-period crossover study comparing the pharmacokinetics of the test product Lansoprazole 30 mg Gastro-Resistant Capsules versus the reference product Prezal (lansoprazole) 30 mg gastro-resistant capsules (Aventis Pharma BV, The Netherlands) in healthy subjects under fasting conditions.

Subjects were dosed with either treatment after at least a 10-hour fast. Blood sampling was performed pre- and up to 12 hours post dose in each treatment period. The washout period between the two treatment arms was at least 7 days. Pharmacokinetic parameters were measured from plasma and statistically analysed.

The pharmacokinetic results for lansoprazole (presented as mean, standard deviation (SD), ratios and 90% confidence intervals) are presented below:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Test</th>
<th>Reference</th>
<th>Test/Ref Ratio</th>
<th>90% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AUC_{0-t} (ng/ml h)</strong></td>
<td>2828.631</td>
<td>2964.252</td>
<td>95.696%</td>
<td>87.172 – 105.055</td>
</tr>
<tr>
<td>SD</td>
<td>1513.961</td>
<td>1420.667</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>AUC_{0-inf} (ng/ml h)</strong></td>
<td>2857.836</td>
<td>2999.356</td>
<td>95.628%</td>
<td>87.178 – 104.896</td>
</tr>
<tr>
<td>SD</td>
<td>1541.620</td>
<td>1461.219</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>C_{max} (ng/ml)</strong></td>
<td>1222.397</td>
<td>1144.050</td>
<td>104.622%</td>
<td>93.902 – 116.567</td>
</tr>
<tr>
<td>SD</td>
<td>485.699</td>
<td>395.314</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

AUC\textsubscript{0-t} = area under the plasma concentration-time curve from time zero to t hours

AUC\textsubscript{0-inf} = area under the plasma concentration-time curve from time zero to infinity

C\textsubscript{max} = maximum plasma concentration

90% geometric CI calculated from ln-transformed data

Study 2
A randomised, open-label, single-dose, two-period crossover study comparing the pharmacokinetics of the test product Lansoprazole 30 mg Gastro-Resistant Capsules versus the reference product Opiren (lansoprazole) 30 mg gastro-resistant capsules (Almirall Prodesfarma, Spain) in healthy subjects under fed conditions.

Subjects were dosed with either treatment after an overnight fast followed by a standard continental breakfast. Blood sampling was performed pre- and up to 12 hours post dose in each treatment period. Standard meals were served 6 and 12 hours post dosing. The washout period between the two treatment arms was at least 7 days. Pharmacokinetic parameters were measured from plasma and statistically analysed.

The pharmacokinetic results for lansoprazole (presented as mean, standard deviation (SD), ratios and 90% confidence intervals) are presented below:
### Table 2. Pharmacokinetic parameters for lansoprazole in fed subjects

<table>
<thead>
<tr>
<th></th>
<th>Test</th>
<th>Reference</th>
<th>Test/Ref Ratio</th>
<th>90% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AUC&lt;sub&gt;0-t&lt;/sub&gt; (ng/ml h)</strong></td>
<td>1602.77</td>
<td>1657.64</td>
<td>101.445%</td>
<td>92.779 – 110.092</td>
</tr>
<tr>
<td>SD</td>
<td>747.004</td>
<td>924.601</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>AUC&lt;sub&gt;0-inf&lt;/sub&gt; (ng/ml h)</strong></td>
<td>1640.76</td>
<td>1690.18</td>
<td>101.296%</td>
<td>92.735 – 110.648</td>
</tr>
<tr>
<td>SD</td>
<td>799.997</td>
<td>955.555</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>C&lt;sub&gt;max&lt;/sub&gt; (ng/ml)</strong></td>
<td>620.118</td>
<td>671.527</td>
<td>95.301%</td>
<td>86.067 – 105.526</td>
</tr>
<tr>
<td>SD</td>
<td>204.342</td>
<td>264.506</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**AUC<sub>0-t</sub>** area under the plasma concentration-time curve from time zero to t hours

**AUC<sub>0-inf</sub>** area under the plasma concentration-time curve from time zero to infinity

**C<sub>max</sub>** maximum plasma concentration

90% geometric CI calculated from ln-transformed data

In both the fed and fasted studies, the 90% confidence interval of the test/reference ratio of geometric means for AUC<sub>0-t</sub>, AUC<sub>0-inf</sub> and C<sub>max</sub> for lansoprazole lie within the acceptable limits. Thus, the data support the claim that the test product is bioequivalent to the reference product.

As the 15 mg and 30 mg strength products meet all the criteria specified in the *Notes for Guidance on the Investigation of Bioavailability and Bioequivalence* (CPMP/EWP/QWP/1401/98), the results and conclusions from the bioequivalence studies with the 30 mg capsule strength can be extrapolated to the 15 mg capsule strength. Both products used in the bioequivalence studies can be considered to be the same as the UK reference product, thus bioequivalence has also been shown between the proposed products and Zoton 15mg and 30mg Capsules.

### EFFICACY

No new data on the efficacy have been submitted and none are required for these types of applications.

### SAFETY

No new or unexpected safety issues were raised by the bioequivalence data.

### PHARMACOVIGILANCE SYSTEM AND RISK MANAGEMENT PLAN

The Pharmacovigilance System, as described by the applicant, fulfils the requirements and provides adequate evidence that the applicant has the services of a qualified person responsible for pharmacovigilance, and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

A suitable justification has been provided for not submitting a risk management plan for these products.

### SUMMARY OF PRODUCT CHARACTERISTICS (SmPC), PATIENT INFORMATION LEAFLET (PIL) AND LABELS

The SmPCs, PIL and labels are medically acceptable. The SmPCs are consistent with those for the originator products.

### CLINICAL EXPERT REPORT

The clinical expert report has been written by an appropriately qualified physician and is a suitable summary of the clinical aspects of the dossier.
CONCLUSION
The grant of Marketing Authorisations is recommended.
OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

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

NON-CLINICAL
No new non-clinical data were submitted and none are required for applications of this type.

EFFICACY
Bioequivalence has been demonstrated between the applicant’s Lansoprazole 30 mg Gastro-Resistant Capsules and its respective reference product. As both strengths of the product meet the criteria specified in the Notes for Guidance on the Investigation of Bioavailability and Bioequivalence (CPMP/EWP/QWP/1401/98), the results and conclusions of the bioequivalence study with the 30 mg capsule strength can be extrapolated to the 15 mg strength.

SAFETY
No new or unexpected safety concerns arise from these applications.

PRODUCT LITERATURE
The SmPCs, PIL and labelling are satisfactory and consistent with those for the reference products, where appropriate.

BENEFIT-RISK ASSESSMENT
The quality of the products is acceptable, and no new non-clinical or clinical safety concerns have been identified. The bioequivalence studies support the claim that the applicant’s products and the originator products are interchangeable. Extensive clinical experience with lansoprazole is considered to have demonstrated the therapeutic value of the compound. The benefit-risk is, therefore, considered to be positive.
LANSOPRAZOLE 15 MG GASTRO-RESISTANT CAPSULES  
LANSOPRAZOLE 30 MG GASTRO-RESISTANT CAPSULES  

PL 14017/0183-6  

**STEPS TAKEN FOR ASSESSMENT**

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<tbody>
<tr>
<td>1</td>
<td>The MHRA received the marketing authorisation applications on 12/10/2009.</td>
</tr>
<tr>
<td>2</td>
<td>Following standard checks and communication with the applicant the MHRA considered the applications valid on 22/10/2009.</td>
</tr>
<tr>
<td>3</td>
<td>Following assessment of the applications, the MHRA requested further information relating to the clinical dossiers on 10/02/2010 and 03/06/2010, and the quality dossiers on 16/03/2010, 14/07/2010 and 17/09/2010.</td>
</tr>
<tr>
<td>4</td>
<td>The applicant responded to the MHRA’s requests, providing further information on the clinical dossiers on 05/05/2010 and 14/10/2010, and the quality dossiers on 16/06/2010, 06/08/2010 and 08/10/2010.</td>
</tr>
<tr>
<td>5</td>
<td>The applications were determined on 24/11/2010.</td>
</tr>
</tbody>
</table>
SUMMARY OF PRODUCT CHARACTERISTICS

Please note that the SmPCs below are the versions for the products that will be marketed in the UK:

1 NAME OF THE MEDICINAL PRODUCT
Lansoprazole 15 mg Gastro-Resistant Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each capsule contains 15 mg of lansoprazole

Excipient(s): Each 15 mg capsule contains 100.474 mg of sucrose

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Gastro-Resistant Capsule, hard

Opaque yellow cap and body capsules. Each capsule contains white or almost white spherical microgranules.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
• Treatment of duodenal and gastric ulcer
• Treatment of reflux oesophagitis
• Prophylaxis of reflux oesophagitis
• Treatment of NSAID-associated benign gastric and duodenal ulcers in patients requiring continued NSAID treatment
• Prophylaxis of NSAID-associated gastric ulcers and duodenal ulcers in patients at risk (see section 4.2) requiring continued therapy
• Symptomatic gastroesophageal reflux disease
• Zollinger-Ellison syndrome.

4.2 Posology and method of administration
For optimal effect, Lansoprazole Gastro-Resistant Capsules should be taken once daily in the morning, except when used for H. pylori eradication when treatment should be twice a day, once in the morning and once in the evening.

Lansoprazole Gastro-Resistant Capsules should be taken at least 30 minutes before food (see section 5.2). Capsules should be swallowed whole with liquid.

For patients with difficulty swallowing; studies and clinical practice suggest that the capsules may be opened and the granules mixed with a small amount of water, apple/tomato juice or sprinkled onto a small amount of soft food (e.g. yoghurt, apple puree) to ease administration. Capsules may also be opened and granules mixed with 40 ml of apple juice for administration through a nasogastric tube (see section 5.2). After preparing the suspension or mixture, the drug should be administered immediately.

Treatment of duodenal ulcer:
The recommended dose is 30 mg once daily for 2 weeks. In patients not fully healed within this time, the medication is continued at the same dose for another two weeks.

Treatment of gastric ulcer:
The recommended dose is 30 mg once daily for 4 weeks. The ulcer usually heals within 4 weeks, but in patients not fully healed within this time, the medication may be continued at the same dose for another 4 weeks.

Reflux oesophagitis:
The recommended dose is 30 mg once daily for 4 weeks. In patients not fully healed within this time, the treatment may be continued at the same dose for another 4 weeks.
Prophylaxis of reflux oesophagitis:
15 mg once daily. The dose may be increased up to 30 mg daily as necessary.

Treatment of NSAID associated benign gastric and duodenal ulcers in patients requiring continued NSAID treatment:
30 mg once daily for four weeks. In patients not fully healed the treatment may be continued for another four weeks. For patients at risk or with ulcers that are difficult to heal, a longer course of treatment and/or a higher dose should probably be used.

Prophylaxis of NSAID associated gastric and duodenal ulcers in patients at risk (such as age > 65 or history of gastric or duodenal ulcer) requiring prolonged NSAID treatment:
15 mg once daily. If the treatment fails the dose 30 mg once daily should be used.

Symptomatic gastro-oesophageal reflux disease:
The recommended dose is 15 mg or 30 mg daily. Relief of symptoms is obtained rapidly. Individual adjustment of dosage should be considered. If the symptoms are not relieved within 4 weeks with a daily dose of 30 mg, further examinations are recommended.

Zollinger-Ellison syndrome:
The recommended initial dose is 60 mg once daily. The dose should be individually adjusted and the treatment should be continued for as long as necessary. Daily doses of up to 180 mg have been used. If the required daily dose exceeds 120 mg, it should be given in two divided doses.

Impaired hepatic or renal function:
There is no need for a dose adjustment in patients with impaired renal function.

Patients with moderate or severe liver disease should be kept under regular supervision and a 50% reduction of the daily dose is recommended (see section 4.4 and 5.2).

Elderly:
Due to reduced clearance of lansoprazole in the elderly an adjustment of dose may be necessary based on individual requirements. A daily dose of 30 mg should not be exceeded in the elderly unless there are compelling clinical indications.

Children:
The use of Lansoprazole Gastro-Resistant Capsules is not recommended in children as clinical data are limited (see also section 5.2).

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients.
Lansoprazole should not be administered with atazanavir (see section 4.5).

4.4 Special warnings and precautions for use
In common with other anti-ulcer therapies, the possibility of malignant gastric tumour should be excluded when treating a gastric ulcer with lansoprazole because lansoprazole can mask the symptoms and delay the diagnosis.

Lansoprazole should be used with caution in patients with moderate and severe hepatic dysfunction (see sections 4.2 and 5.2).

Decreased gastric acidity due to lansoprazole might be expected to increase gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with lansoprazole may lead to a slightly increased risk of gastrointestinal infections such as Salmonella and Campylobacter.

In patients suffering from gastro-duodenal ulcers, the possibility of H. pylori infection as an etiological factor should be considered.

Because of limited safety data for patients on maintenance treatment for longer than 1 year, regular review of the treatment and a thorough risk/benefit assessment should regularly be performed in these patients.
Very rarely cases of colitis have been reported in patients taking lansoprazole. Therefore, in the case of severe and/or persistent diarrhoea, discontinuation of therapy should be considered.

The treatment for the prevention of peptic ulceration of patients in need of continuous NSAID treatment should be restricted to high risk patients (e.g. previous gastrointestinal bleeding, perforation or ulcer, advanced age, concomitant use of medication known to increase the likelihood of upper GI adverse events [e.g. corticosteroids or anticoagulants], the presence of a serious co-morbidity factor or the prolonged use of NSAID maximum recommended doses).

As Lansoprazole Gastro-Resistant Capsules contain sucrose, patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Effects of lansoprazole on other drugs

Medicinal products with pH dependent absorption

Lansoprazole may interfere with the absorption of drugs where gastric pH is critical to bioavailability.

Atazanavir:
A study has shown that co-administration of lansoprazole (60 mg once daily) with atazanavir 400 mg to healthy volunteers resulted in a substantial reduction in atazanavir exposure (approximately 90% decrease in AUC and C_max). Lansoprazole should not be co-administered with atazanavir (see section 4.3).

Ketoconazole and itraconazole:
The absorption of ketoconazole and itraconazole from the gastrointestinal tract is enhanced by the presence of gastric acid. Administration of lansoprazole may result in sub-therapeutic concentrations of ketoconazole and itraconazole and the combination should be avoided.

Digoxin:
Co-administration of lansoprazole and digoxin may lead to increased digoxin plasma levels. The plasma levels of digoxin should therefore be monitored and the dose of digoxin adjusted if necessary when initiating and ending lansoprazole treatment.

Medicinal products metabolised by P450 enzymes

Lansoprazole may increase plasma concentrations of drugs that are metabolised by CYP3A4. Caution is advised when combining lansoprazole with drugs which are metabolised by this enzyme and have a narrow therapeutic window.

Theophylline:
Lansoprazole reduces the plasma concentration of theophylline, which may decrease the expected clinical effect at the dose. Caution is advised when combining the two drugs.

Tacrolimus:
Co-administration of lansoprazole increases the plasma concentrations of tacrolimus (a CYP3A and P-gp substrate). Lansoprazole exposure increased the mean exposure of tacrolimus by up to 81%. Monitoring of tacrolimus plasma concentrations is advised when concomitant treatment with lansoprazole is initiated or ended.

Medicinal products transported by P-glycoprotein

Lansoprazole has been observed to inhibit the transport protein, P-glycoprotein (P-gp) in vitro. The clinical relevance of this is unknown.

Effects of other drugs on lansoprazole

Drugs which inhibit CYP2C19

Fluvoxamine:
A dose reduction may be considered when combining lansoprazole with the CYP2C19 inhibitor fluvoxamine. The plasma concentrations of lansoprazole increase up to 4-fold.
Drugs which induces CYP2C19 and CYP3A4
Enzyme inducers affecting CYP2C19 and CYP3A4 such as rifampicin, and St John’s wort (*Hypericum perforatum*) can markedly reduce the plasma concentrations of lansoprazole.

Others
Sucralfate/Antacids:
Sucralfate/Antacids may decrease the bioavailability of lansoprazole. Therefore lansoprazole should be taken at least 1 hour after taking these drugs.

No clinically significant interactions of lansoprazole with nonsteroidal anti-inflammatory drugs have been demonstrated, although no formal interactions studies have been performed.

4.6 Pregnancy and lactation

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

Therefore, the use of lansoprazole during pregnancy is not recommended.

**Lactation:**
It is not known whether lansoprazole is excreted in human breast milk. Animal studies have shown excretion of lansoprazole in milk.

A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with lansoprazole should be made taking into account the benefit of breastfeeding to the child and the benefit of lansoprazole therapy to the woman.

4.7 Effects on ability to drive and use machines
Adverse drug reactions such as dizziness, vertigo, visual disturbances and somnolence may occur (see section 4.8). Under these conditions the ability to react may be decreased.

4.8 Undesirable effects

Frequencies are defined as Very common (≥1/10), Common (≥1/100 to < 1/10), Uncommon (≥1/1,000 to < 1/100), Rare (≥1/10,000 to <1/1,000), Very rare (<1/10,000), not known (cannot be estimated from the available data).

<table>
<thead>
<tr>
<th>Blood and lymphatic system disorders</th>
<th>Common</th>
<th>Uncommon</th>
<th>Rare</th>
<th>Very rare</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Thrombocytopenia, eosinophilia, leucopenia</td>
<td>Anaemia</td>
<td>Agranulocytosis, pancytopenia</td>
</tr>
<tr>
<td>Psychiatric Disorders</td>
<td></td>
<td>Depression</td>
<td>Insomnia, hallucination, confusion</td>
<td></td>
</tr>
<tr>
<td>Nervous system Disorders</td>
<td>Headache, dizziness</td>
<td>Restlessness, vertigo, paresthesia, somnolence, tremor</td>
<td></td>
<td></td>
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<tr>
<td>Eye disorders</td>
<td>Nausea, diarrhoea, stomach ache, constipation, vomiting, flatulence, dry mouth</td>
<td>Visual disturbances</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal Disorders</td>
<td>Nausea, diarrhoea, stomach ache, constipation, vomiting, flatulence, dry mouth</td>
<td>Glossitis, candidiasis of the oesophagus, pancreatitis, taste disturbances</td>
<td>Colitis, stomatitis</td>
<td></td>
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<tr>
<td>Disorder Type</td>
<td>Symptom</td>
<td></td>
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<td>----------------------------------------</td>
<td>--------------------------------------------------------------------------</td>
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<tr>
<td>Hepatobiliary Disorders</td>
<td>Increase in liver enzyme levels</td>
<td></td>
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<tr>
<td></td>
<td>Hepatitis, jaundice</td>
<td></td>
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<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td>Urticaria, itching, rash</td>
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<td>Petechiae, purpura, hair loss, erythema multiforme, photosensitivity</td>
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<td>Steven-Johnson syndrome, toxic epidermal necrolysis</td>
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<td>Arthralgia, myalgia</td>
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<td>General disorders and administration site conditions</td>
<td>Fatigue, oedema, fever, hyperhidrosis, angioedema, anorexia, impotence</td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Increase in cholesterol and triglyceride levels, hyponatremia</td>
<td></td>
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</tr>
</tbody>
</table>

4.9 **Overdose**

The effects of overdose on lansoprazole in humans are not known (although the acute toxicity is likely to be low) and, consequently, instruction for treatment cannot be given. However, daily doses of up to 180 mg of lansoprazole orally and up to 90 mg of lansoprazole intravenously have been administered in trials without significant undesirable effects.

Please refer to section 4.8 for possible symptoms of lansoprazole overdose.

In the case of suspected overdose the patient should be monitored. Lansoprazole is not significantly eliminated by haemodialysis. If necessary, gastric emptying, charcoal and symptomatic therapy is recommended.

5 **PHARMACOLOGICAL PROPERTIES**

5.1 **Pharmacodynamic properties**

Pharmacotherapeutic group: Proton pump inhibitors, ATC code: A02BC03

Lansoprazole is a gastric proton pump inhibitor. It inhibits the final stage of gastric acid formation by inhibiting the activity of H⁺/K⁺ ATPase of the parietal cells in the stomach. The inhibition is dose-dependent and reversible, and the effect applies to both basal and stimulated secretion of gastric acid.

Lansoprazole is concentrated in the parietal cells and becomes active in their acidic environment, whereupon it reacts with the sulphydryl group of H⁺/K⁺ ATPase causing inhibition of the enzyme activity.

Effect on gastric acid secretion:

Lansoprazole is a specific inhibitor of the parietal cell proton pump. A single oral dose of lansoprazole inhibits pentagastrin-stimulated gastric acid secretion by about 80%. After repeated daily administration for seven days, about 90% inhibition of gastric acid secretion is achieved. It has
a corresponding effect on the basal secretion of gastric acid. A single oral dose of 30 mg reduces
basal secretion by about 70%, and the patients’ symptoms are consequently relieved starting from the
very first dose. After eight days of repeated administration the reduction is about 85%. A rapid relief
of symptoms is obtained by one capsule (30 mg) daily, and most patients with duodenal ulcer
recover within 2 weeks, patients with gastric ulcer and reflux oesophagitis within 4 weeks. By
reducing gastric acidity, lansoprazole creates an environment in which appropriate antibiotics can be
effective against *H. pylori*.

5.2 Pharmacokinetic properties
Lansoprazole is a racemate of two active enantiomers that are biotransformed into the active form in
the acidic environment of the parietal cells. As lansoprazole is rapidly inactivated by gastric acid, it
is administered orally in enteric-coated form(s) for systemic absorption.

Absorption and distribution
Lansoprazole exhibits high (80-90%) bioavailability with a single dose. Peak plasma levels occur
within 1.5 to 2.0 hours. Intake of food slows the absorption rate of lansoprazole and reduces the
bioavailability by about 50%. The plasma protein binding is 97%.

Studies have shown that granules from opened capsules give equivalent AUC as the intact capsule if
the granules are suspended in a small amount of orange juice, apple juice, or tomato juice mixed
with a tablespoon of apple or pear puree or sprinkled on a tablespoon of yoghurt, pudding or cottage
cheese. Equivalent AUC has also been shown for granules suspended in apple juice administered
through a naso-gastric tube.

Metabolism and elimination
Lansoprazole is extensively metabolised by the liver and the metabolites are excreted by both the
renal and biliary route. The metabolism of lansoprazole is mainly catalysed by the enzyme
CYP2C19. The enzyme CYP3A4 also contributes to the metabolism. 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. Sulphone, sulphide and 5-
hydroxyl derivatives of lansoprazole have been identified in plasma. These metabolites have very
little or no antisecretory activity.

A study with 14C labelled lansoprazole indicated that approximately one-third of the administered
radiation was excreted in the urine and two-thirds was recovered in the faeces.

Pharmacokinetics in elderly patients
The clearance of lansoprazole is decreased in the elderly, with elimination half-life increased
approximately 50% to 100%. Peak plasma levels were not increased in the elderly.

Pharmacokinetics in paediatric patients
The evaluation of the pharmacokinetics in children aged 1 –17 years of age showed a similar
exposure as compared to adults with doses of 15 mg for those below 30 kg of weight and 30 mg for
those above. The investigation of a dose of 17 mg/m² body surface or 1 mg/kg body weight also
resulted in comparable exposure of lansoprazole in children aged 2-3 months up to one year of age
compared to adults.

Higher exposure to lansoprazole in comparison to adults has been seen in infants below the age of
2-3 months with doses of both 1.0 mg/kg and 0.5 mg/kg body weight given as a single dose.

Pharmacokinetics in hepatic insufficiency
The exposure of lansoprazole is doubled in patients with mild hepatic impairment and much more
increased in patients with moderate and severe hepatic impairment.

CYP2C19 poor metabolisers
CYP2C19 is subject to genetic polymorphism and 2-6 % of the population, called poor metabolisers
(PMs), are homozygote for a mutant CYP2C19 allele and therefore lacks a functional CYP2C19
enzyme. The exposure of lansoprazole is several-fold higher in PMs than in extensive metabolisers
(EMs).
5.3 **Preclinical safety data**

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

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

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

The clinical relevance of these findings is unknown.

6 **PHARMACEUTICAL PARTICULARS**

6.1 **List of excipients**

Sugar spheres (sucrose and maize starch)
Sodium laurilsulfate
Megumine
Mannitol (E421)
Hyprromellose
Macrogol 6000
Talc
Polyisorbate 80
Titanium dioxide (E171)
Methacrylic Acid-Ethyl Acrylate Copolymer (1:1), Dispersion 30%
Capsule shell:
Gelatin
Titanium dioxide (E171)
Quinoline yellow (E104)

6.2 **Incompatibilities**

Not applicable.

6.3 **Shelf life**

2 years

6.4 **Special precautions for storage**

Do not store above 25°C
Store in the original package in order to protect from moisture.

6.5 **Nature and contents of container**

Aluminium/Aluminium blister. Packs contains 28 capsules.

6.6 **Special precautions for disposal**

No special requirements.

7 **MARKETING AUTHORISATION HOLDER**

Dexcel-Pharma Ltd.
1 Cottesbrooke Park,
Heartlands Business Park,
Daventry, Northamptonshire,
NN11 8YL, UK

8 **MARKETING AUTHORISATION NUMBER(S)**

PL 14017/0183
PL 14017/0185
9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
24/11/2010

10 DATE OF REVISION OF THE TEXT
24/11/2010
1 NAME OF THE MEDICINAL PRODUCT
Lansoprazole 30 mg Gastro-Resistant Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each capsule contains 30 mg of lansoprazole
Excipient(s): Each 30 mg capsule contains 200.949 mg of sucrose
For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Gastro-Resistant Capsule, hard
Opaque white cap and body capsules. Each capsule contains white or almost white spherical microgranules.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
• Treatment of duodenal and gastric ulcer
• Treatment of reflux oesophagitis
• Prophylaxis of reflux oesophagitis
• Treatment of NSAID-associated benign gastric and duodenal ulcers in patients requiring continued NSAID treatment
• Prophylaxis of NSAID-associated gastric ulcers and duodenal ulcers in patients at risk (see section 4.2) requiring continued therapy
• Symptomatic gastroesophageal reflux disease
• Zollinger-Ellison syndrome.

4.2 Posology and method of administration
For optimal effect, Lansoprazole Gastro-Resistant Capsules should be taken once daily in the morning, except when used for *H. pylori* eradication when treatment should be twice a day, once in the morning and once in the evening.
Lansoprazole Gastro-Resistant Capsules should be taken at least 30 minutes before food (see section 5.2). Capsules should be swallowed whole with liquid.
For patients with difficulty swallowing; studies and clinical practice suggest that the capsules may be opened and the granules mixed with a small amount of water, apple/tomato juice or sprinkled onto a small amount of soft food (e.g. yoghurt, apple puree) to ease administration. Capsules may also be opened and granules mixed with 40 ml of apple juice for administration through a nasogastric tube (see section 5.2). After preparing the suspension or mixture, the drug should be administered immediately.

**Treatment of duodenal ulcer:**
The recommended dose is 30 mg once daily for 2 weeks. In patients not fully healed within this time, the medication is continued at the same dose for another two weeks.

**Treatment of gastric ulcer:**
The recommended dose is 30 mg once daily for 4 weeks. The ulcer usually heals within 4 weeks, but in patients not fully healed within this time, the medication may be continued at the same dose for another 4 weeks.

**Reflux oesophagitis:**
The recommended dose is 30 mg once daily for 4 weeks. In patients not fully healed within this time, the treatment may be continued at the same dose for another 4 weeks.

**Prophylaxis of reflux oesophagitis:**
15 mg once daily. The dose may be increased up to 30 mg daily as necessary.

**Treatment of NSAID associated benign gastric and duodenal ulcers in patients requiring continued NSAID treatment:**
30 mg once daily for four weeks. In patients not fully healed the treatment may be continued for another four weeks. For patients at risk or with ulcers that are difficult to heal, a longer course of treatment and/or a higher dose should probably be used.
Prophylaxis of NSAID associated gastric and duodenal ulcers in patients at risk (such as age > 65 or history of gastric or duodenal ulcer) requiring prolonged NSAID treatment:
15 mg once daily. If the treatment fails the dose 30 mg once daily should be used.

Symptomatic gastro-oesophageal reflux disease:
The recommended dose is 15 mg or 30 mg daily. Relief of symptoms is obtained rapidly. Individual adjustment of dosage should be considered. If the symptoms are not relieved within 4 weeks with a daily dose of 30 mg, further examinations are recommended.

Zollinger-Ellison syndrome:
The recommended initial dose is 60 mg once daily. The dose should be individually adjusted and the treatment should be continued for as long as necessary. Daily doses of up to 180 mg have been used. If the required daily dose exceeds 120 mg, it should be given in two divided doses.

Impaired hepatic or renal function:
There is no need for a dose adjustment in patients with impaired renal function.
Patients with moderate or severe liver disease should be kept under regular supervision and a 50% reduction of the daily dose is recommended (see section 4.4 and 5.2).

Elderly:
Due to reduced clearance of lansoprazole in the elderly an adjustment of dose may be necessary based on individual requirements. A daily dose of 30 mg should not be exceeded in the elderly unless there are compelling clinical indications.

Children:
The use of Lansoprazole Gastro-Resistant Capsules is not recommended in children as clinical data are limited (see also section 5.2).

4.3 Contraindications
Hypersensitivity to the active substance or to any of the excipients.
Lansoprazole should not be administered with atazanavir (see section 4.5).

4.4 Special warnings and precautions for use
In common with other anti-ulcer therapies, the possibility of malignant gastric tumour should be excluded when treating a gastric ulcer with lansoprazole because lansoprazole can mask the symptoms and delay the diagnosis.
Lansoprazole should be used with caution in patients with moderate and severe hepatic dysfunction (see sections 4.2 and 5.2).
Decreased gastric acidity due to lansoprazole might be expected to increase gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with lansoprazole may lead to a slightly increased risk of gastrointestinal infections such as Salmonella and Campylobacter.
In patients suffering from gastro-duodenal ulcers, the possibility of H. pylori infection as an etiological factor should be considered.

Because of limited safety data for patients on maintenance treatment for longer than 1 year, regular review of the treatment and a thorough risk/benefit assessment should regularly be performed in these patients.

Very rarely cases of colitis have been reported in patients taking lansoprazole. Therefore, in the case of severe and/or persistent diarrhoea, discontinuation of therapy should be considered.
The treatment for the prevention of peptic ulceration of patients in need of continuous NSAID treatment should be restricted to high risk patients (e.g. previous gastrointestinal bleeding, perforation or ulcer, advanced age, concomitant use of medication known to increase the likelihood of upper GI adverse events [e.g. corticosteroids or anticoagulants], the presence of a serious co-morbidity factor or the prolonged use of NSAID maximum recommended doses).
As Lansoprazole Gastro-Resistant Capsules contain sucrose, patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction
Effects of lansoprazole on other drugs
**Medicinal products with pH dependent absorption**

Lansoprazole may interfere with the absorption of drugs where gastric pH is critical to bioavailability.

**Atazanavir:**
A study has shown that co-administration of lansoprazole (60 mg once daily) with atazanavir 400 mg to healthy volunteers resulted in a substantial reduction in atazanavir exposure (approximately 90% decrease in AUC and Cmax). Lansoprazole should not be co-administered with atazanavir (see section 4.3).

**Ketoconazole and itraconazole:**
The absorption of ketoconazole and itraconazole from the gastrointestinal tract is enhanced by the presence of gastric acid. Administration of lansoprazole may result in sub-therapeutic concentrations of ketoconazole and itraconazole and the combination should be avoided.

**Digoxin:**
Co-administration of lansoprazole and digoxin may lead to increased digoxin plasma levels. The plasma levels of digoxin should therefore be monitored and the dose of digoxin adjusted if necessary when initiating and ending lansoprazole treatment.

**Medicinal products metabolised by P450 enzymes**

Lansoprazole may increase plasma concentrations of drugs that are metabolised by CYP3A4. Caution is advised when combining lansoprazole with drugs which are metabolised by this enzyme and have a narrow therapeutic window.

**Theophylline:**
Lansoprazole reduces the plasma concentration of theophylline, which may decrease the expected clinical effect at the dose. Caution is advised when combining the two drugs.

**Tacrolimus:**
Co-administration of lansoprazole increases the plasma concentrations of tacrolimus (a CYP3A and P-gp substrate). Lansoprazole exposure increased the mean exposure of tacrolimus by up to 81%. Monitoring of tacrolimus plasma concentrations is advised when concomitant treatment with lanzoprazole is initiated or ended.

**Medicinal products transported by P-glycoprotein**

Lansoprazole has been observed to inhibit the transport protein, P-glycoprotein (P-gp) *in vitro*. The clinical relevance of this is unknown.

**Effects of other drugs on lansoprazole**

**Drugs which inhibit CYP2C19**
Fluvoxamine:
A dose reduction may be considered when combining lansoprazole with the CYP2C19 inhibitor fluvoxamine. The plasma concentrations of lansoprazole increase up to 4-fold.

**Drugs which induces CYP2C19 and CYP3A4**
Enzyme inducers affecting CYP2C19 and CYP3A4 such as rifampicin, and St John’s wort (*Hypericum perforatum*) can markedly reduce the plasma concentrations of lansoprazole.

**Others**
Sucralfate/Antacids:
Sucralfate/Antacids may decrease the bioavailability of lansoprazole. Therefore lansoprazole should be taken at least 1 hour after taking these drugs.

No clinically significant interactions of lansoprazole with nonsteroidal anti-inflammatory drugs have been demonstrated, although no formal interactions studies have been performed.

**4.6 Pregnancy and lactation**

**Pregnancy:**
For lansoprazole no clinical data on exposed pregnancies are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development. Therefore, the use of lansoprazole during pregnancy is not recommended.

**Lactation:**
It is not known whether lansoprazole is excreted in human breast milk. Animal studies have shown excretion of lansoprazole in milk.

A decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with lansoprazole should be made taking into account the benefit of breastfeeding to the child and the benefit of lansoprazole therapy to the woman.
### 4.7 Effects on ability to drive and use machines

Adverse drug reactions such as dizziness, vertigo, visual disturbances and somnolence may occur (see section 4.8). Under these conditions the ability to react may be decreased.

### 4.8 Undesirable effects

Frequencies are defined as Very common (≥1/10), Common (≥1/100 to < 1/10), Uncommon (≥1/1,000 to < 1/100), Rare (≥1/10,000 to <1/1,000), Very rare (<1/10,000), not known (cannot be estimated from the available data).

<table>
<thead>
<tr>
<th>Common</th>
<th>Uncommon</th>
<th>Rare</th>
<th>Very rare</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood and lymphatic system disorders</td>
<td>Thrombocytopenia, eosinophilia, leucopenia</td>
<td>Anaemia</td>
<td>Agranulocytosis, pancytopenia</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td>Depression</td>
<td>Insomnia, hallucination, confusion</td>
<td></td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td>Headache, dizziness</td>
<td>Restlessness, vertigo, paresthesia, somnolence, tremor</td>
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4.9 Overdose
The effects of overdose on lansoprazole in humans are not known (although the acute toxicity is likely to be low) and, consequently, instruction for treatment cannot be given. However, daily doses of up to 180 mg of lansoprazole orally and up to 90 mg of lansoprazole intravenously have been administered in trials without significant undesirable effects.
Please refer to section 4.8 for possible symptoms of lansoprazole overdose. In the case of suspected overdose the patient should be monitored. Lansoprazole is not significantly eliminated by haemodialysis. If necessary, gastric emptying, charcoal and symptomatic therapy is recommended.

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Proton pump inhibitors, ATC code: A02BC03
Lansoprazole is a gastric proton pump inhibitor. It inhibits the final stage of gastric acid formation by inhibiting the activity of H⁺/K⁺ ATPase of the parietal cells in the stomach. The inhibition is dose-dependent and reversible, and the effect applies to both basal and stimulated secretion of gastric acid. Lansoprazole is concentrated in the parietal cells and becomes active in their acidic environment, whereupon it reacts with the sulphydryl group of H⁺/K⁺ ATPase causing inhibition of the enzyme activity.
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5.2 Pharmacokinetic properties
Lansoprazole is a racemate of two active enantiomers that are biotransformed into the active form in the acidic environment of the parietal cells. As lansoprazole is rapidly inactivated by gastric acid, it is administered orally in enteric-coated form(s) for systemic absorption.
Absorption and distribution
Lansoprazole exhibits high (80-90%) bioavailability with a single dose. Peak plasma levels occur within 1.5 to 2.0 hours. Intake of food slows the absorption rate of lansoprazole and reduces the bioavailability by about 50%. The plasma protein binding is 97%.
Studies have shown that granules from opened capsules give equivalent AUC as the intact capsule if the granules are suspended in a small amount of orange juice, apple juice, or tomato juice mixed with a tablespoon of apple or pear puree or sprinkled on a tablespoon of yoghurt, pudding or cottage cheese. Equivalent AUC has also been shown for granules suspended in apple juice administered through a naso-gastric tube.
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Lansoprazole is extensively metabolised by the liver and the metabolites are excreted by both the renal and biliary route. The metabolism of lansoprazole is mainly catalysed by the enzyme CYP2C19. The enzyme CYP3A4 also contributes to the metabolism. 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. Sulphone, sulphide and 5-hydroxyl derivatives of lansoprazole have been identified in plasma. These metabolites have very little or no antisecretory activity.
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The clearance of lansoprazole is decreased in the elderly, with elimination half-life increased approximately 50% to 100%. Peak plasma levels were not increased in the elderly.
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Higher exposure to lansoprazole in comparison to adults has been seen in infants below the age of 2-3 months with doses of both 1.0 mg/kg and 0.5 mg/kg body weight given as a single dose.

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The exposure of lansoprazole is doubled in patients with mild hepatic impairment and much more increased in patients with moderate and severe hepatic impairment.

CYP2C19 poor metabolisers
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Preclinical data reveal no special hazards for humans based on conventional studies of safety pharmacology, repeated dose toxicity, toxicity to reproduction or genotoxicity.
In two rat carcinogenicity studies, lansoprazole produced dose-related gastric ECL cell hyperplasia and ECL cell carcinoids associated with hypergastrinaemia due to inhibition of acid secretion. Intestinal metaplasia was also observed, as were Leydig cell hyperplasia and benign Leydig cell tumours. After 18 months of treatment retinal atrophy was observed. This was not seen in monkeys, dogs or mice.
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The clinical relevance of these findings is unknown.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
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Mannitol (E421)
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Polysorbate 80
Titanium dioxide (E171)
Methacrylic Acid-Ethyl Acrylate Copolymer (1:1), Dispersion 30%

Capsule shell:
Gelatin
Titanium dioxide (E171)

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
2 years

6.4 Special precautions for storage
Do not store above 25°C
Store in the original package in order to protect from moisture.

6.5 Nature and contents of container
Aluminium/Aluminium blister. Packs contains 28 capsules.
6.6 Special precautions for disposal
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NN11 8YL, UK

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PL 14017/0184
PL 14017/0186

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
24/11/2010

10 DATE OF REVISION OF THE TEXT
24/11/2010
Please note that the Patient information leaflets below are the versions for the products that will be marketed in the UK:

Lansoprazole 15 mg Gastro-Resistant Capsules
(Lansoprazole)

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 any further questions, ask your doctor or pharmacist.
• This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
• If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

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. How to store Lansoprazole Capsules
6. Further information

1. WHAT LANSOPRAZOLE CAPSULES ARE AND WHAT THEY ARE USED FOR
   The name of your medicine is Lansoprazole 15mg Gastro-Resistant Capsules (called Lansoprazole Capsules throughout this leaflet).
   The active ingredient in Lansoprazole Capsules is lansoprazole, which is a proton pump inhibitor. Proton pump inhibitors reduce the amount of acid that your stomach makes.

   Your doctor may prescribe Lansoprazole Capsules for the following indications:
   • Treatment of duodenal and stomach ulcer
   • Treatment of inflammation in your oesophagus (reflux oesophagitis)
   • Prevention of reflux oesophagitis
   • Treatment of heartburn and acid reumination
   • Treatment or prevention of duodenal or stomach ulcer in patients requiring continued NSAID treatment (NSAID treatment is used against pain or inflammation)
   • Treatment of Zollinger-Ellison syndrome

2. BEFORE YOU TAKE LANSOPRAZOLE CAPSULES
   Do not take Lansoprazole Capsules:
   • If you are allergic (hypersensitive) to lansoprazole or any of the other ingredients of Lansoprazole Capsules
   • If you are taking a medicine containing the active substance atazanavir (used in the treatment of HIV)

   Take special care with Lansoprazole Capsules
   • If you have serious liver disease. The doctor may have to adjust your dosage.
   • If diarrhoea occurs during the treatment with Lansoprazole Capsules contact your doctor immediately, as lansoprazole has been associated with a small increase in infectious diarrhoea. If your doctor has given you Lansoprazole Capsules in addition to other medicines intended for the treatment of Helicobacter pylori infection (antibiotics) or together with anti-inflammatory medicines to treat your pain or rheumatic disease; please also read the package leaflets of these medicines carefully.
   • If you take Lansoprazole Capsules on a long-term basis (longer than 1 year) your doctor will probably keep you under regular surveillance. You should report any new and exceptional symptoms and circumstances whenever you see your doctor.

   If you think any of these apply to you or you are unsure, talk to your doctor or pharmacist before taking lansoprazole. Do this even if they applied only in the past.
Taking other medicines
Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

In particular tell your doctor if you are taking medicines containing any of the following active substances as Lansoprazole Capsules may affect the way these drugs work:
- ketoconazole, itraconazole, rifampicin (used to treat infections)
- digoxin (used to treat heart problems)
- theophylline (used to treat asthma)
- tacrolimus (used to prevent transplant rejection)
- fluvoxamine (used to treat depression and other psychiatric diseases)
- antacids (used to treat heartburn or acid regurgitation)
- sucralfate (used for healing ulcers)
- St John’s wort (Hypericum perforatum) (used to treat mild depression)

Taking Lansoprazole Capsules with food and drink
For the best results from your medicine you should take Lansoprazole Capsules at least 30 minutes before food.

Pregnancy and breast-feeding
If you are pregnant, breast-feeding or if there is a chance you might be pregnant ask your doctor for advice before taking this medicine.

Driving and using machines
Side effects such as dizziness, vertigo, tiredness and visual disturbances sometimes occur in patients taking lansoprazole. If you experience side effects like these you should take caution as your ability to react may be decreased.

You alone are responsible to decide if you are in a fit condition to drive a motor vehicle or perform other tasks that demand increased concentration. Because of their effects or undesirable effects, one of the factors that can reduce your ability to do these things safely is your use of medicines.

Descriptions of these effects can be found in other sections. Read all the information in this leaflet for guidance.

Discuss with your doctor, nurse or pharmacist if you are unsure about anything.

Important information about some of the ingredients of Lansoprazole Capsules
Lansoprazole Capsules contain sucrose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. HOW TO TAKE Lansoprazole CAPSULES

Always take Lansoprazole capsules exactly as your doctor has told you. The dose will depend on your needs and the illness being treated. Check with your doctor or pharmacist if you are not sure.

Swallow the capsule whole with a glass of water. If you find the capsule difficult to swallow your doctor may advise on alternative ways to take your medicine. Do not crush or chew these capsules or the content of an emptied capsule because this will stop them from working properly.

If you are taking Lansoprazole Capsules once a day, try to take it at the same time each day. You may get best results if you take Lansoprazole Capsules first thing in the morning.

If you are taking Lansoprazole Capsules twice a day, you should have the first dose in the morning and the second dose in the evening.

The dose of Lansoprazole Capsules depends on your condition. The usual doses of Lansoprazole Capsules for adults are given below. Your doctor will sometimes prescribe you a different dose and will tell you how long your treatment will last.

Treatment of heartburn and acid regurgitation: 15 mg or 30 mg once daily for 4 weeks. If symptoms persist you should report to your doctor. If your symptoms are not relieved within 4 weeks, please contact your doctor.

Treatment of duodenal ulcer: 30 mg once daily for 2 weeks

Treatment of stomach ulcer: 30 mg once daily for 4 weeks

Treatment of inflammation in your oesophagus (reflux oesophagitis): 30 mg once daily for 4 weeks

Long-term prevention of reflux oesophagitis: 15 mg once daily, your doctor may adjust your dose to 30 mg once daily.
If you are being treated for infection because you have an ulcer, it is unlikely that your ulcer will return if the infection is successfully treated. To give your medicine the best chance of working, take it at the right time and do not miss a dose.

Treatment of duodenal or stomach ulcer in patients requiring continued NSAID treatment: 30 mg once daily for 4 weeks.

Prevention of duodenal or stomach ulcer in patients requiring continued NSAID treatment: one 15 mg once daily, your doctor may adjust your dose to one 30 mg once daily.

Zollinger-Ellison syndrome: The usual dose is 60 mg every day to start with, then depending on how you respond to Lansoprazole Capsules the dose that your doctor decides is best for you.

Lansoprazole Capsules should not be given to children.
Take your medicine exactly as your doctor has told you. You should check with your doctor if you are not sure how to take your medicine.

If you take more Lansoprazole Capsules than you should
If you take more Lansoprazole Capsules than you have been told to, seek medical advice quickly.

If you forget to take Lansoprazole Capsules
If you forget to take a dose, take it as soon as you remember unless it is nearly time for your next dose. If this happens skip the missed dose and take the remaining capsules as normal. Do not take a double dose to make up for a forgotten capsule.

If you stop taking Lansoprazole Capsules
Do not stop treatment early because your symptoms have got better. Your condition may not have been fully healed and may reoccur if you do not finish your course of treatment.

If you have any further questions on the use of this product, ask your doctor.

4. POSSIBLE SIDE EFFECTS
Like all medicines, Lansoprazole Capsules can cause side effects, although not everybody gets them.

Stop taking Lansoprazole and see a doctor or go to a hospital straightaway if:
- You get swelling of the hands, feet, ankles, face, lips or throat which may cause difficulty in swallowing or breathing. You could also notice an itchy, lumpy rash (hives) or nettle rash (urticaria)
  This may mean you are having an allergic reaction to Lansoprazole capsules.
- You have blistering, peeling or bleeding of the skin around the lips, eyes, mouth, nose and genitals.
  You may also have flu-like symptoms and a high temperature. These could be signs of something called Stevens-Johnson syndrome.
- You get a severe blistering rash in which layers of the skin may peel off to leave large areas of raw exposed skin over the body.
- You get symptoms such as: yellowing of your skin or whites of your eyes, tiredness and fever. This may be due to inflammation of the liver or changes in the way your liver is working.

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

Tell your doctor as soon as possible if:
- You get long lasting diarrhoea and keep being sick. This can happen because Lansoprazole lowers the natural acid in your stomach which would normally help to kill the bacteria there. This, in turn, can lead to stomach infections.
- You have changes in passing water (urine). This may be due to kidney problems or changes in the way your kidneys are working.
- You bruise more easily than usual or you get more infections than usual. This could be due to a blood problem.

The following side effects are common (occur in more than 1 in 100 patients):
- headache, dizziness
- diarrhoea, constipation, stomach pains, feeling or being sick, wind, dry or sore mouth or throat
- skin rash, itching
- changes in liver function test values
- tiredness
The following side effects are uncommon (occur in less than 1 in 100 patients):
- depression
- joint or muscle pain
- fluid retention or swelling
- changes in blood cell counts

The following side effects are rare (occur in less than 1 in 1000 patients):
- fever
- restlessness, drowsiness, confusion, hallucinations, insomnia, visual disturbances, vertigo
- a change in the way things taste, loss of appetite, inflammation of your tongue (glossitis)
- skin reactions such as burning or prickling feeling under the skin, blisters, reddening and excessive sweating
- sensitivity to light
- hair loss
- feelings of ants creeping over the skin (paresthesiae), trembling
- anaemia (paleness)
- kidney problems
- pancreatitis
- inflammation of the liver (may be seen as yellow skin or eyes)
- breast swelling in males, impotence
- candidiasis (fungal infection, may affect skin or the mucosa)
- angioedema; You should see your doctor immediately if you experience symptoms of angioedema, such as swollen face, tongue or pharynx, difficulty to swallow, hives and difficulties to breath

The following side effects are very rare (occur in less than 1 in 10000 patients):
- severe hypersensitivity reactions including shock. Symptoms of a hypersensitivity reaction may include
  - fever, rash, swelling and sometimes a fall in blood pressure
  - inflammation of your mouth (stomatitis)
  - colitis (bowel inflammation)
  - changes in test values such as sodium, cholesterol and triglyceride levels
  - very severe skin reactions with reddening, blistering, severe inflammation and skin loss.
  - very rarely Lansoprazole Capsules may cause a reduction in the number of white blood cells and your resistance to infection may be decreased. If you experience an infection with symptoms such as fever and serious deterioration of your general condition, or fever with local infection symptoms such as sore throat/pharynx/mouth or urinary problems you should see your doctor immediately. A blood test will be taken to check possible reduction of white blood cells (agranulocytosis)

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

5. HOW TO STORE LANSOPRAZOLE CAPSULES
Keep out of the reach and sight of children.
Do not use Lansoprazole Capsules after the expiry date which is stated on the blister and carton (Exp.).
The expiry date refers to the last day of that month.
Do not store above 25°C. Store in the original package in order to protect from moisture.
Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION
What Lansoprazole Capsules contain
The active substance is Lansoprazole.
Each capsule of Lansoprazole 15 mg Gastro-Resistant Capsules contains 15mg Lansoprazole.
The other ingredients are:
Capsule content: Sugar spheres (sucrose and maize starch), Sodium laurylsulfate, Magnelumine, Mannitol (E:421), Hypromellose, Macrogol 6000, Talc, Polysorbate 80, Titanium dioxide (E171), Methacrylic Acid-Ethyl Acrylate Copolymer (1:1), Dispersion 30%,
Capsule shell: Gelatin, Titanium dioxide (E171), Quinoline yellow (E104)

What Lansoprazole Capsules look like and contents of the pack
Lansoprazole 15 mg Gastro-Resistant Capsules are opaque yellow capsules. Lansoprazole Capsules are available in packs containing 28 capsules.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder: Dexcel®-Pharma Ltd. 1 Cottesbrooke Park, Heartlands Business Park, Daventry, Northamptonshire, NN11 8YL, UK
Manufacturer:
LABORATORIOS LICOMSA, S.A. Avda. Miralcampo, N°7, Polígono Industrial Miralcampo, 19200 Azuqueca de Henares (Guadalajara), Spain

This leaflet was last approved in November 2010.

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Lansoprazole 30 mg Gastro-Resistant Capsules
(Lansoprazole)

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 any further questions, ask your doctor or pharmacist.
• This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
• If any of the side effects get serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

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. How to store Lansoprazole Capsules
6. Further information

1. WHAT LANSOPRAZOLE CAPSULES ARE AND WHAT THEY ARE USED FOR
The name of your medicine is Lansoprazole 30mg Gastro-Resistant Capsules (called Lansoprazole Capsules throughout this leaflet).
The active ingredient in Lansoprazole Capsules is lansoprazole, which is a proton pump inhibitor. Proton pump inhibitors reduce the amount of acid that your stomach makes.
Your doctor may prescribe Lansoprazole Capsules for the following indications:
• Treatment of duodenal and stomach ulcer
• Treatment of inflammation in your oesophagus (reflux oesophagitis)
• Prevention of reflux oesophagitis
• Treatment of haemorrhage and acid reactivation
• Treatment or prevention of duodenal or stomach ulcer in patients requiring continued NSAID treatment (NSAID treatment is used against pain or inflammation)
• Treatment of Zollinger-Ellison syndrome

2. BEFORE YOU TAKE LANSOPRAZOLE CAPSULES
Do not take Lansoprazole Capsules:
• If you are allergic (hypersensitive) to lansoprazole or any of the other ingredients of Lansoprazole Capsules
• If you are taking a medicine containing the active substance atazanavir (used in the treatment of HIV)

Take special care with Lansoprazole Capsules
• If you have serious liver disease. The doctor may have to adjust your dosage.
• If diarrhoea occurs during the treatment with Lansoprazole Capsules contact your doctor immediately, as lansoprazole has been associated with a small increase in infectious diarrhoea. If your doctor has given you Lansoprazole Capsules in addition to other medicines intended for the treatment of Helicobacter pylori infection (antibiotics) or together with anti-inflammatory medicines to treat your pain or rheumatic disease; please also read the package leaflets of these medicines carefully.
• If you take Lansoprazole Capsules on a long-term basis (longer than 1 year) your doctor will probably keep you under regular surveillance. You should report any new and exceptional symptoms and circumstances whenever you see your doctor.

If you think any of these apply to you or you are unsure, talk to your doctor or pharmacist before taking lansoprazole. Do this even if they applied only in the past.
Taking other medicines
Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

In particular tell your doctor if you are taking medicines containing any of the following active substances as Lansoprazole Capsules may affect the way these drugs work:
- ketoconazole, itraconazole, rifampicin (used to treat infections)
- digoxin (used to treat heart problems)
- theophylline (used to treat asthma)
- tacrolimus (used to prevent transplant rejection)
- fluvoxamine (used to treat depression and other psychiatric diseases)
- antacids (used to treat heartburn or acid regurgitation)
- sucralfate (used for healing ulcers)
- St John’s wort (Hypericum perforatum) (used to treat mild depression)

Taking Lansoprazole Capsules with food and drink
For the best results from your medicine you should take Lansoprazole Capsules at least 30 minutes before food.

Pregnancy and breast-feeding
If you are pregnant, breast-feeding or if there is a chance you might be pregnant ask your doctor for advice before taking this medicine.

Driving and using machines
Side effects such as dizziness, vertigo, tiredness and visual disturbances sometimes occur in patients taking Lansoprazole. If you experience side effects like these you should take caution as your ability to react may be decreased.

You alone are responsible to decide if you are in a fit condition to drive a motor vehicle or perform other tasks that demand increased concentration. Because of their effects or undesirable effects, one of the factors that can reduce your ability to do these things safely is your use of medicines.

Descriptions of these effects can be found in other sections.

Read all the information in this leaflet for guidance.
Discuss with your doctor, nurse or pharmacist if you are unsure about anything.

Important Information about some of the ingredients of Lansoprazole Capsules
Lansoprazole Capsules contain sucrrose. If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. HOW TO TAKE LANSOPRAZOLE CAPSULES
Always take Lansoprazole capsules exactly as your doctor has told you. The dose will depend on your needs and the illness being treated. Check with your doctor or pharmacist if you are not sure.

Swallow the capsule whole with a glass of water. If you find the capsules difficult to swallow your doctor may advise on alternative ways to take your medicine. Do not crush or chew these capsules or the content of an emptied capsule because this will stop them from working properly.

If you are taking Lansoprazole capsules once a day, try to take it at the same time each day. You may get best results if you take Lansoprazole Capsules first thing in the morning.

If you are taking Lansoprazole Capsules twice a day, you should have the first dose in the morning and the second dose in the evening.

The dose of Lansoprazole Capsules depends on your condition. The usual doses of Lansoprazole Capsules for adults are given below. Your doctor will sometimes prescribe you a different dose and will tell you how long your treatment will last.

Treatment of heartburn and acid regurgitation: 15 mg or 30 mg once daily for 4 weeks. If symptoms persist you should report to your doctor. If your symptoms are not relieved within 4 weeks, please contact your doctor.

Treatment of duodenal ulcer: 30 mg once daily for 2 weeks
Treatment of stomach ulcer: 30 mg once daily for 4 weeks
Treatment of inflammation in your oesophagus (reflux oesophagitis): 30 mg once daily for 4 weeks

Long-term prevention of reflux oesophagitis: 15 mg once daily, your doctor may adjust your dose to 30 mg once daily.
If you are being treated for infection because you have an ulcer, it is unlikely that your ulcer will return if the infection is successfully treated. To give your medicine the best chance of working, take it at the right time and do not miss a dose.

Treatment of duodenal or stomach ulcer in patients requiring continued NSAID treatment: 30 mg once daily for 4 weeks.

Prevention of duodenal or stomach ulcer in patients requiring continued NSAID treatment: one 15 mg once daily, your doctor may adjust your dose to one 30 mg once daily.

Zollinger-Ellison syndrome: The usual dose is 60 mg every day to start with, then depending on how you respond to Lansoprazole Capsules the dose that your doctor decides is best for you.

Lansoprazole Capsules should not be given to children.
Take your medicine exactly as your doctor has told you. You should check with your doctor if you are not sure how to take your medicine.

If you take more Lansoprazole Capsules than you should
If you take more Lansoprazole Capsules than you have been told to, seek medical advice quickly.

If you forget to take Lansoprazole Capsules
If you forget to take a dose, take it as soon as you remember unless it is nearly time for your next dose. If this happens skip the missed dose and take the remaining capsules as normal. Do not take a double dose to make up for a forgotten capsule.

If you stop taking Lansoprazole Capsules
Do not stop treatment early because your symptoms have got better. Your condition may not have been fully healed and may reoccur if you do not finish your course of treatment.

If you have any further questions on the use of this product, ask your doctor.

4. POSSIBLE SIDE EFFECTS
Like all medicines, Lansoprazole Capsules can cause side effects, although not everybody gets them.

Stop taking Lansoprazole and see a doctor or go to a hospital straightaway if:
• You get swelling of the hands, feet, ankles, face, lips or throat which may cause difficulty in swallowing or breathing. You could also notice an itchy, lumpy rash (hives) or nettle rash (urticaria). This may mean you are having an allergic reaction to Lansoprazole capsules.
• You have blisters, peeling or bleeding of the skin around the lips, eyes, mouth, nose and genitals.
• You may also have flu-like symptoms and a high temperature. These could be signs of something called Stevens-Johnson syndrome
• You get a severe blistering rash in which layers of the skin may peel off to leave large areas of raw exposed skin over the body
• You get symptoms such as: yellowing of your skin or whites of your eyes, tiredness and fever. This may be due to inflammation of the liver or changes in the way your liver is working

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

Tell your doctor as soon as possible if:
• You get long lasting diarrhoea and keep being sick. This can happen because Lansoprazole lowers the natural acid in your stomach which would normally help to kill the bacteria there. This, in turn, can lead to stomach infections
• You have changes in passing water (urine). This may be due to kidney problems or changes in the way your kidneys are working
• You bruise more easily than usual or you get more infections than usual. This could be due to a blood problem

The following side effects are common (occur in more than 1 in 100 patients):
• headache, dizziness
• diarrhoea, constipation, stomach pains, feeling or being sick, wind, dry or sore mouth or throat
• skin rash, itching
• changes in liver function test values
• tiredness
The following side effects are uncommon (occur in less than 1 in 100 patients):
- depression
- joint or muscle pain
- fluid retention or swelling
- changes in blood cell counts

The following side effects are rare (occur in less than 1 in 1000 patients):
- fever
- restlessness, drowsiness, confusion, hallucinations, insomnia, visual disturbances, vertigo
- a change in the way things taste, loss of appetite, inflammation of your tongue (glossitis)
- skin reactions such as burning or prickling feeling under the skin, bruising, reddening and excessive sweating
- sensitivity to light
- hair loss
- feelings of ants creeping over the skin (paresthesiae), trembling
- anaemia (paleness)
- kidney problems
- pancreatitis
- inflammation of the liver (may be seen as yellow skin or eyes)
- breast swelling in males, impotence
- candidiasis (fungal infection, may affect skin or the mucosa)
- angioedema; You should see your doctor immediately if you experience symptoms of angioedema, such as swollen face, tongue or pharynx, difficulty to swallow, hives and difficulties to breath

The following side effects are very rare (occur in less than 1 in 10000 patients):
- severe hypersensitivity reactions including shock. Symptoms of a hypersensitivity reaction may include fever, rash, swelling and sometimes a fall in blood pressure
- inflammation of your mouth (stomatitis)
- colitis (bowel inflammation)
- changes in test values such as sodium, cholesterol and triglyceride levels
- very severe skin reactions with reddening, blistering, severe inflammation and skin loss
- very rarely Lansoprazole Capsules may cause a reduction in the number of white blood cells and your resistance to infection may be decreased. If you experience an infection with symptoms such as fever and serious deterioration of your general condition, or fever with local infection symptoms such as sore throat/pharynx/mouth or urinary problems you should see your doctor immediately. A blood test will be taken to check possible reduction of white blood cells (agranulocytosis)

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

5. HOW TO STORE LANSOPRAZOLE CAPSULES
Keep out of the reach and sight of children.
Do not use Lansoprazole Capsules after the expiry date which is stated on the blister and carton (Exp.).
The expiry date refers to the last day of that month.
Do not store above 25°C. Store in the original package in order to protect from moisture.
Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION
What Lansoprazole Capsules contain
The active substance is Lansoprazole.
Each capsule of Lansoprazole 30 mg Gastro-Resistant Capsules contains 30mg Lansoprazole.
The other ingredients are:
Capsule content: Sugar spheres (sucrose and maize starch), Sodium laurylsulfate, Megilumine, Mannitol (E421), Hypromellose, Macrogol 6000, Talc, Polysorbate 80, Titanium dioxide (E171), Methacrylic Acid-Ethyl Acrylate Copolymer (1:1), Dispersion 30%
Capsule shell: Gelatin, Titanium dioxide (E171)

What Lansoprazole Capsules look like and contents of the pack
Lansoprazole 30 mg Gastro-Resistant Capsules are opaque white capsules.
Lansoprazole Capsules are available in packs containing 28 capsules.

Marketing Authorisation Holder and Manufacturer
Marketing Authorisation Holder: Dexca®-Pharma Ltd. 1 Cottesbrooke Park, Heartlands Business Park, Daventry, Northamptonshire, NN11 8YL, UK

Manufacturer:
LABORATORIOS LICONSIA, S.A. Avda. Miralcalno, N°7, Poligono Industrial Miralcalno, 19200 Azuqueca de Henares (Guadalajara), Spain

This leaflet was last approved in November 2010.
Labelling

Carton:

LANSOPRAZOLE 15mg
GASTRO-RESISTANT
CAPSULES

LANSOPRAZOLE 15mg
GASTRO-RESISTANT
CAPSULES

LANSOPRAZOLE 15mg
GASTRO-RESISTANT
CAPSULES

LANSOPRAZOLE 15mg
GASTRO-RESISTANT
CAPSULES

Each capsule contains 15 mg Lansoprazole. Also contains sucrose. See package leaflet for
further information.

Dosage: For oral use. Do not crush or chew. Take as directed by your doctor.

Read the package leaflet before use.

Do not store above 25°C. Store in the original package in order to protect from moisture.

KEEP OUT OF THE REACH AND SIGHT OF CHILDREN.

POM

PL 14017/0183

MARKETING AUTHORISATION HOLDER:

Dexcel® PHARMA LTD.,
1 COTEBROOK PARK, YEATES AND BUSINESS PARK,
DARTSLAND, NORTHAMPTONSHIRE NN11 8YL, UK.

Dexcel®
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