SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Lansoprazol 15 mg capsules gastro-resistant capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 15 mg of lansoprazole

For a full list of excipients, see section 6.1.

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

3 PHARMACEUTICAL FORM

Lansoprazol 15 mg: opaque yellow cap and body capsules. Each capsule contains white or almost white spherical microgranules.

4.1 Therapeutic indications

Lansoprazol 15 mg capsules gastro-resistant capsules are indicated for use in adults,

- Treatment of duodenal and gastric ulcer
- Treatment of oesophagitis by reflux
- Prevention of reflux oesophagitis
- Eradication of *Helicobacter pylori* (*H. pylori*) by concomitant administration of antibiotic appropriate for treatment of ulcers associated with *H. pylori*
- Treatment of duodenal ulcers and benign gastric ulcer, induced by NSAIDs in patients requiring continued NSAID treatment
- Prevention of NSAID-induced duodenal and gastric ulcers in at risk patients (see section 4.2) requiring continued therapy
- Symptomatic gastroesophageal reflux
- Zollinger-Ellison syndrome.

4.2 Posology and method of administration

Treatment of duodenal ulcer:

The recommended dose is 30 mg once daily for 2 weeks. In patients whose healed is not complete after this period, treatment will be continued at the same dosage, for an additional 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 whose healing is not complete after this period, treatment may be continued at the same dosage, for an additional 4 weeks.

Reflux oesophagitis:

The recommended dose is 30 mg once daily for 4 weeks. In patients whose recovery is not complete after this period, the treatment may be continued at the same dose for an additional 4 weeks.

Prophylaxis of reflux oesophagitis:

15 mg once daily. The dose may be increased up to 30 mg daily as necessary.

Eradication of *Helicobacter pylori:*

The choice of appropriate combination therapy should be made according to official local recommendations regarding bacterial resistance, duration of treatment, (usually 7 days but sometimes up to 14 days), and appropriate use of antibacterial agents.

The recommended dose is 30 mg of Lansoprazole twice daily for 7 days in combination with one of the following:

clarithromycin 250-500 mg twice daily + 1 g of amoxicillin twice daily

clarithromycin 250 mg twice daily + metronidazole 400-500 mg twice daily

Eradication rates of *H. pylori* up to 90%, are achieved when clarithromycin is combined with Lansoprazole gasto-resistant capsules and amoxicillin or metronidazole.

Six months after successful eradication treatment, the risk of re-infection is low and relapse is therefore unlikely.

The use of a dose comprising lansoprazole 30 mg twice daily, amoxicillin 1 g twice daily and metronidazole 400-500 mg twice daily has also been studied. Using this combination, lower eradication rates were observed than for dosages involving clarithromycin. They can be adapted for patients who cannot take clarithromycin as part of an eradication therapy, when local resistance rates to metronidazole are low.

Treatment of NSAID induced duodenal ulcers and benign gastric ulcer in patients requiring continued NSAID treatment:

30 mg once daily for four weeks. In patients whose healing is not complete, the treatment may be continued for an additional 4 weeks. In 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.

Prevention of NSAIDs induced duodenal and gastric ulcers in at risk patients (over 65 years of age, or with history of gastric or duodenal ulcer) requiring prolonged NSAIDs 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 achieved quickly. Individual dose adjustment should be considered. If the symptoms are not relieved within 4 weeks with a daily dose of 30 mg, further examinations are recommended.

Syndrome de Zollinger-Ellison:

The recommended initial dose is 60 mg once daily. The dosage should be adjusted individually 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.

Special population

Renal function:

No dose adjustment is required in patients with renal impairment.

Hepatic Impaired

Patients with moderate or severe liver disease should be kept under regular monitoring 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 subjects, individual dose adjustment may be necessary. A daily dose of 30 mg should not be exceeded in the elderly unless there are relevant clinical indications.

Paediatric population:

In the absence of sufficient clinical data, the use of Lansoprazol is not recommended in children (see section 5.2) and the relevance to humans of the results of studies in juvenile animals is unknown (see section 5.3).
Treatment in infants less than one year of age should be avoided as the available clinical data have not demonstrated a beneficial effects of lansoprazole in the treatment of gastro-oesophageal reflux disease.

Mode of administration

For optimal effect, Lansoprazole should be taken once daily in the morning, except in the case of radication *H. pylori* for which treatment should be twice a day, once in the morning and once in the evening.
Lansoprazole should be taken at least 30 minutes before meals (see section 5.2). Capsules should be swallowed whole with liquid.
For patients with swallowing difficulty; 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 sauce) to facilitated administration. The capsules may also be opened and the microgranules 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.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Malignant gastric tumor

As with other anti-ulcer treatments, the possibility of malignant gastric tumour should be rule out when treating a gastric ulcer with lansoprazole as lansoprazole can mask the symptoms and delay the diagnosis.

Concomitant administration of HIV protease inhibitors
The combination of lansoprazole with pH-dependent HIV protease inhibitors such as atazanavir and nelfinavir is not recommended due to the very significant decrease in their bioavailability (see section 4.5).
Hypomagnesaemia
Severe hypomagnesaemia has been reported rarely in patients treated with proton pump inhibitors (PPIs) such as lansoprazole for at least three months, and in most cases for one year. Hypomagnesaemia can manifest itself by severe clinical sign such as fatigue, tetany, delirious flushing, convulsions, dizziness and ventricular arrhythmia, but it can begin insidiously and go unnoticed. Hypomagnesaemia may result in hypocalcaemia and/or hypokalaemia (see section 4.8). In most patients, hypomagnesaemia (and hypomagnesaemia associated with hypocalcaemia and/or hypokalaemia) improved after magnesium supplementation and PPI discontinuation.
In patients requiring prolonged treatment or in case of combination of PUPs with digoxin or with medicinal products that may cause hypomagnesaemia (e.g., diuretics), blood magnesium testing should be considered by health care professionals prior to initiation of PPI therapy and then regularly during treatment.
Influence on the absorption of vitamin B_{12}
Daily treatment with any acid-suppressing medications over a prolonged period of time (several years) may lead to malabsorption of cyanocobalamin (vitamin B12) caused by hypo- or achlorhydria.
This should be taken into account in patients with reduced reserves or with risk factors for decreased absorption of vitaminB12 during long-term treatment or if clinical symptoms are observed.
Hepatic impairment
Lansoprazole should be used with caution in patients with moderate and severe hepatic impairment (see sections 4.2 and 5.2).
Gastrointestinal bacterial infections
Lansoprazole, like other PPI treatments, may be associated with an increased risk of infection with *Clostridium difficile*.
A decreased in gastric acidity due to lansoprazole may increase levels of bacteria normally found in the gastrointestinal tract. Treatment with lansoprazole may lead to a slight increased risk of gastrointestinal infections especially due to *Salmonella* and *Campylobacter*.
Eradication of Helicobacter pylori
In patients with peptic ulcers, the possibility of infection with *H. pylori* as an etiological factor should be considered.
If lansoprazole is used in combination with antibiotics for the eradication treatment of *H.pylori*, then the conditions for the use of these antibiotics should also be followed.
Long term treatment
Due to limited safety data in patients on maintenance therapy for longer than 1 year, regular review of the treatment and a thorough risk/benefit assessment should regularly be performed in these patients.
Colitis
Very rarely cases of colitis have been reported in patients on lansoprazole. Therefore, in the case of severe and/or persistent diarrhoea, discontinuation of therapy should be considered.

Co-administration of NSAIDs
The treatment for the prevention of peptic ulceration of patients requiring continuous treatment with NSAIDs should be limited to patients at high risk (e.g. history of gastrointestinal bleeding, perforation or ulcer, advanced age, concomitant use of medication known to increase the likelihood of adverse events in the upper gastrointestinal tract [e.g. corticosteroids or anticoagulants], presence of a serious co-morbidity factor or the prolonged use of NSAID in maximum recommended doses).
Risk of bone fracture
Proton pump inhibitors, especially if used in high doses and for a prolong period of time (>1 year), may moderately increase the risk of hip, wrist and vertebrae fracture, mainly in the elderly or in the presence of other identified risk factors. Observational studies suggest that proton pump inhibitors may increase the overall risk of fracture by 10–40%. This increase may be partly due to other risk factors. Patients at risk of osteoporosis should managed according to current recommendation and receive an appropriate intake of vitamin D and calcium.
Subacute cutaneous lupus erythematosus (SCLE)

Proton pump inhibitors are associated with very occasional cases of SCLE. If lesions develop, especially on skin areas exposed of the sun, and if they are accompanied by arthralgia, the patient should seek medical attention promptly and the health care professional should consider stopping lansoprazole. The occurrence of SCLE after treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.
Interference with laboratory tests

Increased levels of Chromogranin A (CgA) may interfere with tests performed for the exploration of neuroendocrine tumours. To avoid this interference, treatment with lansoprazole should be discontinoued at least 5 days before measuring CgA level (see section 5.1). If CgA and gastrin levels have not normalized after initial measurement, measurements should be repeated 14 days after discontinuation of proton pump inhibitor therapy.
Loansoprazole gastro-resistance capsule containe sucrose
As Lansoprazole contains sucrose, patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Effects of lansoprazole on other Medicinal product

Medicinal products with pH dependent absorption

Lansoprazole may interfere with the absorption of drugs for which bioavailability depends on gastric pH.
HIV Protease Inhibitors:
Combination not recommended with HIV protease inhibitors for which absorption is dependent on gastric pH, such as atazanavir and nelfinavir, due to the significant decrease in plasma concentration of the protease inhibitor (see section 4.4).

Once study shown that concomitant of lansoprazole (60 mg once daily) and atazanavir 400 mg to healthy volunteers significantly reduction exposure to atazanavir (approximately 90% decrease in AUC (area under curve)and Cmax(Peak concentration)).

Ketoconazole, itraconazole and posaconazole:

The absorption of ketoconazole, itraconazole and posaconazole from the gastrointestinal tract is increased in the presence of stomach acid. Administration of lansoprazole may result in sub-therapeutic concentrations of ketoconazole, itraconazole and posaconazole and the combination should be avoided.

Digoxin:

The combination of lansoprazole and digoxin may result in an increase in plasma digoxin concentration. Digoxin plasma concentration should therefore be monitored and the digoxin dose adjusted if necessary at the start and end of treatment with lansoprazole.

Medicinal products metabolised by cytochrome P450 enzymes

Lansoprazole may increase plasma concentrations of medicinal products metabolised by CYP3A4. Caution is advised when combining lansoprazole with medicinal products metabolised by this enzyme and with a low therapeutic range.

Theophylline:

Lansoprazole reduces the plasma concentration of theophylline, which may decrease the expected clinical effect. Patient monitoring should be taken in account when combining the two drugs.

Tacrolimus:

Concomitant administration of lansoprazole increases plasma concentrations of tacrolimus (a CYP3A and P-gp). Taking lansoprazole increases the average level of tacrolimus by up to 81%.

Monitoring of tacrolimus plasma concentrations is recommended at the start or end of treatment with lanzoprazole. Determination of blood concentrations of tacrolimus, control of renal function and dose adjustment during the combination and after discontinuation.

Medicinal products transported by P-glycoprotein

Inhibition of P-glycoprotein (P-gp) by lansoprazole has been observed *in vitro*. The clinical relevance of this is unknown.

Effects of other medicinal product 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.

Medicine products which induces CYP2C19 and CYP3A4

Enzyme inducers affecting CYP2C19 and CYP3A4 such as rifampicin, and St John´s wort (*Hypericum perforatum*) can significantly reduce the plasma concentrations of lansoprazole.

Risk of ineffectiveness of antisecretory treatment by decreasing its metabolism by St. John's wort to be taken into account.

Others

Sucralfate/Antacids:

Sucralfate and 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 and nonsteroidal antiinflammatory drugs have been demonstrated, although no formal interactions studies have been performed.

Other interactions

Associations not recommended

+ Methotrexate

Risk of increased toxicity of methotrexate by decreasing elimination.

Not recommended in combination with methotrexate at doses > 20 mg/week.

Association to be considered for lower doses.

Associations to consider

+ Cyanocobalamin

Risk of cyanocobalamin deficiency after prolonged treatment (a few years), the reduction of gastric acidity by these drugs may decrease the digestive absorption of vitamin B_{12}.

+ Tyrosine kinase inhibitors

Risk of decreased bioavailability of the tyrosine kinase inhibitor, due to its pH-dependent absorption.

+ Mycophenolate mofetil

Decrease in mycophenolic acid concentrations by about one third, with potential risk of decreased efficacy.

+ Ulipristal

Risk of diminishing the effect of ulipristal by decreasing its absorption.

+ Warfarin

Co-administration of lansoprazole 60 mg and warfarin did not alter the pharmacokinetics of warfarin or INR. However, there have been cases of increased INR and prothrombin time when PPI and warfarin are combined.

Increases in INR and prothrombin time can lead to abnormal bleeding and eventually death. Monitoring of INR and prothrombin time is recommended in patients treated with lansoprazole and warfarin.

4.6 Fertility, pregnancy and lactation

Pregnancy:

There are limited data on the use of lansoprazole in pregnant women. Animal studies have not shown any direct or indirect deleterious effects on pregnancy, embryonic/foetal development, childbirth or postnatal development.

As a precautionary measure, it is best to avoid the use of lansoprazole during pregnancy.

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.

Fertility:

There are no data in humans regarding the effect of lansoprazole on fertility. Reproduction studies in pregnant female rats and rabbits showed no effect of lansoprazole on fertility, no malformative or foetotoxic effect, and no effect in breastfed babies.

4.7 Effects on ability to drive and use machines

Undesirable effects, such as dizziness, visual disturbances and somnolence may occur (see section 4.8). Under these conditions the ability to react may be diminished.

4.8 Undesirable effects

Tabulated list of adverse reactions.
Frequencies are defined as 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).

For all post-marketing adverse reactions, it is not possible to apply any frequency of adverse reactions, so they are reported with an "indeterminate" frequency.
Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

	Common	**Uncommon**	**Rare**	**Very rare**	**Frequency not known**

Hematological and lymphatic system disorders		Thrombo-cytopenia, Eosinophilia, Leucopenia	Anaemia	Agranulocytosis, pancytopenia	
Immune system disorders				Anaphylactic shock	
Metabolism and nutrition disorders					Hyponatremia* Hypomagnesaemia*, hypocalcaemia*#, hypokalaemia*#
Psychiatric Disorders		Depression	Insomnia, Hallucination, confusion		Visual hallucinations
Nervous system Disorders	Headache, dizziness		Impatience, dizziness, Paresthesia, drowsiness, tremor		
Eye disorders			Visual disturbances.		
Gastro-intestinal Disorders	Nausea, diarrhoea, abdominal pain, constipation, vomiting, flatulence, dry mouth or throat, fundic gland polyps (benign)		Glossitis, oesophagus candidiasis, pancreatitis, taste disturbances	Colitis, stomatitis	
Hepatobiliary disorders	Increase in liver enzyme levels		Hepatitis, jaundice		
Skin and subcutaneous tissue disorders	Urticaria, itching, rash		Petechiae, purpura, hair loss, erythema multiforme, photosensitivity	StevenJohnson syndrome, toxic epidermal necrolysis (Lyell syndrome)	Subacute cutaneous lupus erythematosus (see section 4.4)
Musculo-skeletal and connective tissue disorders		Arthralgia, myalgia, Fracture of the hip, wrist or spine (See section 4.4)			
Kidney and urinary disorders			Tubulointerstitial nephritis		
Disorders of the reproductive			Gynaecomastia		

organ and breast					
General disorders and administration site conditions	Fatigue	Oedema	Fever, hyperhidrosis, angioedema, anorexia, impotence		
Investigations				Increase in cholesterol and triglyceride levels, hyponatremia	

** adverse reactions observed after approval of dexlansoprazole (as these reactions are voluntarily reported by a population of uncertain size, their frequency cannot be estimated from the available data)

Hypocalcaemia and/or hypokalaemia may be related to the occurrence of hypomagnesaemia (see section 4.4)

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Yellow Card Scheme: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

The effects of lansoprazole overdose in humans are not known (although the acute toxicity is likely to be low) and, therefore no treatment action can be specified.
However, daily doses of up to 180 mg of lansoprazole orally and up to 90 mg of lansoprazole intravenously have been administered in clinical trials without significant adverse 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.

5.1 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 the proton pump H^+/K^+ ATPase of the parietal cells in the stomach. The inhibition is dose dependent

and reversible. Its effect are exerted on both basal and stimulated of gastric acid secretion.
Lansoprazole is concentrated in the parietal cells and becomes active in their acidic environment and reacts with the hydrogen sulphydryl group of H^+/K^+ATPase causing inhibition of the enzyme activity.
Effect on gastric acid secretion:

Lansoprazole is a specific inhibitor of the proton pump parietal cells. A single oral dose of Lansoprazole inhibits pentagastrin-stimulated gastric acid secretion by about 80%. After repeated daily administration for a period of seven days, about 90% gastric acid secretion is inhibited. It has a similer effect on the basal secretion of gastric acid. A single oral administration of 30 mg reduces basal secretion by about 70%; The patients' symptoms are therefore improved from the first dose. After eight days of repeated administration the reduction is about 85%. A rapid relief of symptoms is achieved with one capsule (30 mg) per day, 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.*
During treatment with antisecretory medicinal products, the serum concentration of gastrin increases in response to the decreased acid secretion. Similarly, CgA increases due to decreased gastric acidity. The increased CgA level may interfere with test performed for the exploration of neuroendocrine tumours.
According to published data, proton pump inhibitors should be discontinued between 5 days and 2 weeks before measuring CgA levels. The goal is to allow a return to normal CgA levels that would have been artificially increased by taking PPIs.

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. Since lansoprazole is rapidly inactivated by gastric acid, it is administered orally in enteric-coated form(s) for systemic absorption.
Absorption and distribution

The bioavailability of lansoprazole as single dose is high (80-90%). Maxium plasma concentrations are reached within 1.5 to 2.0 hours. Intake of food slows the absorption rate of lansoprazole and reduces the bioavailabilty by about 50%. The plasma protein binding is 97%.
Studies have shown that microgranules from opened capsules give an area under curve (AUC) equivalent to the intact capsule if the microgranules are mixed 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. An equivalent AUC was also been found for microgranules mixed with apple juice administered through a naso-gastric tube.
Metabolism and elimination
Lansoprazole is primarily metabolised by the liver and the metabolites are excreted through the renal and biliary tracts. The metabolism of lansoprazole

is primarily catalysed by the enzyme CYP2C19. The enzyme CYP3A4 also contributes to the metabolism. The plasma elimination half-life of lansoproazole is between 1 to 2 hours depending on single or multiple doses in healthy subjects. There is no evidence of accumulation after multiple doses in healthy subjects. The sulfone, sulphide and 5-hydroxyl derivatives of lansoprazole have been identified in plasma. These metabolites have very little or no antisecretory activity.
A study with ^{14}C labelled lansoprazole indicated that approximately one-third of the administered radiation was excreted in the urine and two-thirds was recovered in the faeces.

Special polulation

Elderly

Lansoprazole clearance of is reduced in the elderly subject, with elimination half-life increased approximately 50% to 100%. Maximum plasma concentration are not increased in the elderly.
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/m^2 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 reported in children 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.
Hepatic insufficiency

The exposure of lansoprazole is doubled in patients with mild hepatic impairment and even more increased in patients with moderate and severe hepatic impairment.
Poor metabolisers by CYP2C19

CYP2C19 is subject to genetic polymorphism and 2-6 % of the population, called poor metabolisers (PMs), are homozygote for a allelic mutation CYP2C19 and therefore have a deficiency of the functional enzyme CYP2C19. The exposure of lansoprazole is multiplied several-time in LDs compared to rapid 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 carcinogenicity studies in rats, lansoprazole results in dose-related enterochromaffin gastric cell hyperplasia (LCE) and ECL cell carcinoids associated with hypergastrinaemia related to acid secretion inhibition. Intestinal metaplasia was also observed, as well as hyperplasia of Leydig cell and benign tumours of Leydig cell. After 18 months of treatment retinal atrophy was observed. This was not seen in monkeys, dogs or mice.

In mouse carcinogenicity studies dose-related gastric ECL cell hyperplasia developed as well as liver tumours and adenoma of rete testis.
The clinical relevance of these findings is unknown.

Studies in juvenile animals:

Studies in juvenile rats (8-week study, 6-week dose titration toxicokinetic study, developmental sensitivity study) covering the paediatric population less than 12 years of age showed an increased incidence of heart valve thickening. The results were reversible, or tended towards reversibility, after a 4-week recovery period without medication. Juvenile rats less than 21 days of age (equivalent to about 2 years in humans) were more susceptible to the development of heart valve thickening. The margin of safety from expected exposure to Lansoprazole in humans is in the range of 3 to 6 times the exposure in juvenile animal studies based on AUC at the maximum no-observable effect (NOEL) level (8-week study, 6-week toxicokinetic dose titration study) or lowest observable effect level (LOEL) (developmental sensitivity study).
The relevance of these findings for paediatric patients younger than 12 years of age is unknown.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sugar spheres (sucrose and maize starch)
Sodium laurilsulphate
Meglumine
Mannitol
Hypromellose
Macrogol
Talc
Polysorbate 80
Titanium dioxide (E171)
Methacrylic Acid-Ethyl Acrylate Copolymer, 1:1, Dispersion 30%

Capsule shell:

Gelatin
Titanium dioxide (E171)

Quinoline yellow (E104) – only 15 mg capsules

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store below 25ºC.

Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

Al/Al blister 7, 14, 28, 56 and 98 capsules

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Activase Pharmaceuticals Limited,

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Nicosia.

Cyprus

8 MARKETING AUTHORISATION NUMBER(S)

PL 28444/0037

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