

IRISH MEDICINES BOARD ACT 1995

MEDICINAL PRODUCTS(LICENSING AND SALE)REGULATIONS, 1998

(S.I. No.142 of 1998)

PA0711/089/001

Case No: 2032410

The Irish Medicines Board in exercise of the powers conferred on it by the above mentioned Regulations hereby grants to

Rowex Ltd

Bantry, Co. Cork, Ireland

an authorisation, subject to the provisions of the said Regulations, in respect of the product

Lansoprazole 15 Milligram Capsules Gastro-Resistant

The particulars of which are set out in Part I and Part II of the attached Schedule. The authorisation is also subject to the general conditions as may be specified in the said Regulations as listed on the reverse of this document.

This authorisation, unless previously revoked, shall continue in force from **19/01/2007** until .

Signed on behalf of the Irish Medicines Board this

A person authorised in that behalf by the said Board.

Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Lansoprazole 15mg gastro-resistant capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 15mg Lansoprazole.

For excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Gastro-resistant capsule, hard

Opaque yellow cap and body no. 3 capsule containing white or almost white spherical microgranules.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Uses

Lansoprazole is effective in the treatment of acid-related disorders of the upper gastro-intestinal tract, with the benefit of rapid symptom relief. Lansoprazole is also effective in combination with antibiotics in the eradication of *Helicobacter pylori* (*H. pylori*).

Indications

Healing and long term management of Gastro Oesophageal Reflux Disease (GORD).

Healing and maintenance therapy for patients with duodenal ulcer.

Healing of benign gastric ulcer.

Treatment of Non-Steroidal Anti-Inflammatory Drug (NSAID)-associated benign gastric ulcers and duodenal ulcers in patients requiring continued NSAID treatment.

Prophylaxis of NSAID-associated benign gastric and duodenal ulcers and relief of symptoms.

Treatment of Zollinger-Ellison syndrome.

Lansoprazole is also effective in patients with benign peptic lesions, including reflux oesophagitis, unresponsive to H₂ receptor antagonists.

Eradication of *H. pylori* from the upper gastro-intestinal tract in patients with peptic ulcer (duodenal or benign gastric ulcer) when used in combination with appropriate antibiotics, leading to the healing and prevention of relapse of the ulcer.

4.2 Posology and method of administration

Dosage

Gastro Oesophageal Reflux Disease:

In reflux oesophagitis the recommended dosage is Lansoprazole 30 mg once daily for 4 weeks. The majority of patients will be healed after the first course. For those patients not fully healed at this time, a further 4 weeks treatment at the same dosage should be given.

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

Duodenal ulcer:

The recommended dose is Lansoprazole 30 mg once daily for 4 weeks. For prevention of relapse, the recommended maintenance dose is Lansoprazole 15 mg once daily.

Benign gastric ulcer:

The recommended dose is Lansoprazole 30 mg once daily for 8 weeks.

Maintenance treatment should not continue for more than one year unless considered essential by the prescribing physician.

Zollinger-Ellison Syndrome:

The initial dose should be Lansoprazole 60 mg once daily. The dosage should then be adjusted individually. Treatment should be continued under specialist supervision for as long as clinically indicated.

For patients who require 120 mg or more per day, the dose should be divided and administered twice daily.

Treatment of NSAID-associated benign gastric and duodenal ulcers:

Lansoprazole 15 mg or 30 mg once daily for 4 to 8 weeks. Most patients will be healed after 4 weeks; for those patients not fully healed, a further 4 weeks treatment can be given.

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

Prophylaxis of NSAID-associated benign gastric and duodenal ulcers and relief of symptoms:

Lansoprazole 15 mg or 30 mg once daily.

*Eradication of *H. pylori*:*

The following combinations have been shown to be effective when given for 7 days:

Lansoprazole 30 mg twice daily plus clarithromycin 250-500 mg twice daily and amoxycillin 1 g twice daily, or

Lansoprazole 30 mg twice daily plus clarithromycin 250-500 mg twice daily and metronidazole 400 mg twice daily.

These regimens have eradicated *H. pylori* in 90% of patients.

Eradication of *H. pylori* with any one of the above regimens has been shown to result in the healing of duodenal ulcers, without the need for additional anti-ulcer drug therapy. Further, since the risk of re-infection with *H. pylori* is very low, it follows that relapse of a healed duodenal ulcer following *H. pylori* eradication is unlikely.

Administration

Lansoprazole should be taken once daily, except when used to eradicate *H. pylori*. To achieve the optimal acid

inhibitory effect, and hence most rapid healing and symptom relief, Lansoprazole should be administered in the morning before food.

The capsules should be swallowed whole. Do not crush or chew.

Elderly:

Dose adjustment is not required in the elderly. The normal daily dosage should be given.

Children:

There is no experience with Lansoprazole in children.

Impaired Hepatic and Renal Function:

Lansoprazole is metabolised substantially by the liver. Clinical trials in patients with liver disease indicate that metabolism of lansoprazole is prolonged when daily doses of 30mg are administered to patients with severe hepatic impairment. It is therefore recommended that the daily dose for patients with severe liver disease is individually adjusted to 15mg or 30mg. These patients should be kept under regular supervision and a daily dosage of 30mg should not be exceeded.

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

4.3 Contraindications

The use of Lansoprazole is contra-indicated in patients with a history of hypersensitivity to any of the ingredients of Lansoprazole capsules.

4.4 Special warnings and precautions for use

In common with other anti-ulcer therapies, the possibility of malignancy should be excluded when gastric ulcer is suspected, as symptoms may be alleviated and diagnosis delayed.

Before using Lansoprazole with antibiotics to eradicate *H. pylori*, prescribers should refer to the full prescribing information of the respective antibiotics for guidance.

Maintenance treatment should not continue for more than one year unless considered essential by the prescribing physician.

Lansoprazole should be used with caution in patients with severe hepatic dysfunction. These patients should be kept under regular supervision, and a daily dosage of 30mg should not be exceeded (see section 4.2 Posology and Method of Administration).

Decreased gastric acidity due to any means, including proton pump inhibitors, increases gastric counts of bacteria normally present in the gastrointestinal tract. Treatment with acid-reducing drugs may lead to a slightly increased risk of gastrointestinal infections such as *Salmonella* and *Campylobacter*.

Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Lansoprazole is hepatically metabolised and studies indicate that it is a weak inducer of Cytochrome P450. There is the possibility of interaction with drugs, which are metabolised by the liver. Caution should be exercised when oral contraceptives and preparations such as phenytoin, carbamazepine, theophylline, or warfarin are taken concomitantly with the administration of Lansoprazole.

No clinically significant effects on NSAIDs or diazepam have been found.

Antacids and sucralfate may reduce the bioavailability of lansoprazole and should therefore not be taken within an hour of Lansoprazole.

4.6 Pregnancy and lactation

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

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

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

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

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

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

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

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

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

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

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

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

Gynaecomastia and impotence have been reported rarely.

4.9 Overdose

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC code: A02BC03.

Lansoprazole is a member of a class of drugs called proton pump inhibitors. Its mode of action is to inhibit specifically the H^+/K^+ ATPase (proton pump) of the parietal cell in the stomach, the terminal step in acid production, thus reducing gastric acidity, a key requirement for healing of acid-related disorders such as gastric ulcer duodenal ulcer and reflux oesophagitis. It is believed that the parent drug is biotransformed into its active form(s) in the acidic environment of the parietal cell, whereupon it reacts with the sulphydryl group of the H^+/K^+ ATPase causing inhibition. This inhibition is reversible *in vitro* by intrinsic and extrinsic reducing agents. Lansoprazole's mode of action differs significantly from the H_2 antagonists, which inhibit one of the three pathways involved in stimulation of acid production. A single dose of 30 mg inhibits pentagastrin-stimulated acid secretion by approximately 80%, indicating effective acid inhibition from the first day of dosing.

5.2 Pharmacokinetic properties

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

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

5.3 Preclinical safety data

Gastric carcinoids, localised to the oxyntic mucosa, have been observed in life-long studies in rats. These changes have been related to sustained hypergastrinaemia secondary to acid inhibition and not from a direct effect of any individual drug.

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

No such treatment related changes have been observed in patients treated continuously with Lansoprazole for up to 12 months.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Capsule content

Sucrose
Maize Starch
Sodium Laurilsulfate
Meglumine
Mannitol (E421)
Hypromellose
Macrogol 6000
Talc
Polysorbate 80
Titanium Dioxide
Methacrylic Acid-ethyl acrylate copolymer (1:1) Dispersion 30%

Capsule shell

Quinoline Yellow (E104)

Titanium Dioxide (E171)

Purified Water

Gelatin

6.2 Incompatibilities

Not applicable.

6.3 Shelf Life

3 years.

6.4 Special precautions for storage

Do not store above 30°C.

Store in the original package.

6.5 Nature and contents of container

Alu/Alu blister packs of 10 or 30 capsules and sample packs of 10.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements.

7 MARKETING AUTHORISATION HOLDER

Rowex Ltd.

Bantry

Co. Cork

8 MARKETING AUTHORISATION NUMBER

PA 711/89/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of First Authorisation: 03 March 2006

10 DATE OF REVISION OF THE TEXT