NEW ZEALAND DATA SHEET

LANZOL RELIEF

1. Product Name

Lanzol Relief, 15 mg and 30 mg, modified release capsules.

2. Qualitative and Quantitative Composition

Each capsule contains 15 mg or 30 mg of lansoprazole.

Excipients with known effect: Sugar spheres, heavy magnesium carbonate, sucrose, corn starch, hydroxypropyl cellulose, methacrylic acid-ethyl acetate copolymer, and capsule shell.

Allergen Declaration: Contains phenylalanine, sulfites and sugars.

For the full list of excipients, see section 6.1.

3. Pharmaceutical Form

LANZOL RELIEF 15 mg capsules are presented as white to off-white coloured pellets filled in hard gelatin capsules with a green opaque cap and a green opaque body imprinted with 'MYLAN' over '8015' on both cap and body with black ink.

LANZOL RELIEF 30 mg capsules are presented as white to off-white coloured pellets filled in hard gelatin capsules with a pink opaque cap and a pink opaque body imprinted with 'MYLAN' over '8030' on both cap and body with black ink.

4. Clinical Particulars

4.1 Therapeutic indications

- Healing and long-term management of reflux oesophagitis.
- Healing and maintenance therapy for patients with duodenal ulcer.
- Healing of benign gastric ulcer.
- Lansoprazole is also effective in patients with benign peptic lesions that do not respond to H_2-receptor antagonists.
- Eradication of *H. pylori* from the upper gastrointestinal tract in patients with peptic ulcer or chronic gastritis when used in combination with appropriate antibiotics.

4.2 Dose and method of administration

Dose

Reflux oesophagitis

30 mg lansoprazole once daily for 4 weeks. The majority of patients will be healed after the first course. For patients who have not fully healed within this time, a further 4 weeks treatment using the

same dosage regimen is indicated. For long-term management, a maintenance dose of 15 mg or 30 mg once daily can be used dependent upon patient response.

Duodenal ulcer

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

Gastric ulcer

30 mg lansoprazole once daily for 8 weeks.

Eradication of H. pylori

Eradication of the infection is the single most important therapeutic intervention in patients with *H. pylori* positive peptic ulcer disease. The following combinations have been shown to be effective when used for 7 days: 30 mg twice daily plus **two** of the following antibiotics: amoxicillin 1g twice daily, metronidazole 400 mg twice daily and clarithromycin 250 mg twice daily.

Long-term management

Capsules should only be used in certain situations including:

- In patients who have recurrent peptic ulceration where the pathogenesis of the ulcer is not related to *H. pylori* infection; or
- Where repeated eradication therapy is unsuccessful; or
- Patients who have a past history of perforation or bleeding from an ulcer.

Special populations

Renal impairment

There is no need to alter the dosage in patients with impaired renal function.

Hepatic impairment

Lansoprazole is metabolised substantially by the liver. The results of clinical trials in patients with liver disease indicate that the metabolism of lansoprazole is prolonged in patients with severe hepatic impairment. A 50% reduction in the daily dose is recommended in patients with moderate or severe hepatic impairment.

4.3 Contraindications

Hypersensitivity to lansoprazole or other proton pump inhibitors or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

General

As with other anti-ulcer therapies, the possibilities of malignancy should be excluded when a gastric ulcer is suspected, since treatment with lansoprazole may alleviate the symptoms of a malignancy and possibly delay its diagnosis.

Helicobacter pylori eradication

When using lansoprazole with antibiotics to eradicate *H. pylori*, it is recommended that prescribers refer to the approved product information for the antibiotics selected.

Gastrointestinal Bacterial Infections

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 medicines may lead to a slightly increased risk of gastrointestinal infections such as *Salmonella* and

Campylobacter. Proton pump inhibitor therapy may be associated with an increased risk of *Clostridium difficile* infection.

Influence on Vitamin B12 Absorption

Lansoprazole may decrease the absorption of vitamin B12 (cyanocobalamin) due to hypochlorhydria or achlorhydria. This should be considered in patients with reduced body stores or risk factors for decreased vitamin B12 absorption during long-term treatment or if clinical symptoms are observed.

Enterochromaffin-like cell effects (ECL)

Safety concerns of long term treatment relate to hypergastrinaemia and possible ECL effects. ECL cell hyperplasia and gastric carcinoid tumour were observed in animal studies (see section 5.3).

Human gastric biopsy specimens from patients treated with proton pump inhibitors have not detected ECL cell effects similar to those seen in rats. Gastric biopsies taken in all the long-term maintenance studies have revealed:

- A slight increase in mean endocrine cell count during 12 months maintenance treatment with lansoprazole 15 mg or 30 mg, observed in 3 of 4 studies. Cell density averages were slightly higher under 30 mg lansoprazole than under 15 mg lansoprazole once daily. These observations were reversible approximately 3 months after maintenance therapy stopped in two of the studies.
- Single cases of changes from normal to simple hyperplasia which persisted in one patient 3 months after discontinuation of treatment.
- For antral biopsies a greater mean gastrin-positive cell density and mean serotonin-positive cell density was found for lansoprazole 30 mg compared to lansoprazole 15 mg once daily.
- No evidence of carcinoid tumours or visible endocrine cell proliferation was seen in any patient for either fundus or antral biopsies.

(There are currently biopsy data on over 400 patients treated between 9 months and one year and over 230 patients treated for more than one year.)

Hypomagnesaemia

Severe hypomagnesaemia, symptomatic and asymptomatic, has been reported in patients treated with proton pump inhibitors (PPIs) like lansoprazole for at least 3 months and in most cases for 1 year. Hypomagnesemia can result in severe clinical signs, such as fatigue, delirium, tetany, brief psychotic disorder with marked stressors, seizures, dizziness and ventricular arrhythmia, but onset may be insidious and be overlooked. In some patients, treatment of hypomagnesaemia with magnesium replacement was not sufficient to correct the magnesium imbalance and discontinuation of the PPI was required. In patients later retreated with the same or different PPI, hypomagnesaemia returned within a shorter time period.

Hypomagnesaemia can lead to 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 discontinuation of the PPI.

In patients requiring prolonged treatment or when PPIs are combined with digoxin or medicinal products that may cause hypomagnesaemia (e.g. diuretics), health professionals should consider measuring magnesium levels before starting PPI treatment and periodically during treatment.

Risk of Fractures

Proton pump inhibitors, especially if used in high doses and for a prolonged period (>1 year), may modestly increase the risk of hip, wrist and spine fracture, mainly in the elderly or in presence of other recognised risk factors. Observational studies suggest that proton pump inhibitors may increase the overall risk of fracture by 10–40%. Some of this increase may be due to other risk factors. Patients at risk of osteoporosis should receive care according to current clinical guidelines and they should have an adequate intake of vitamin D and calcium.

Subacute Cutaneous Lupus Erythematosus (SCLE)

Proton pump inhibitors are associated with very infrequent cases of SCLE. If lesions occur, especially in sun-exposed areas of the skin, and if accompanied by arthralgia, the patient should seek medical help promptly and the healthcare professional should consider stopping lansoprazole. SCLE onset after treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.

Retinal atrophy

In animal studies, retinal atrophy was observed in Sprague Dawley rats dosed orally with lansoprazole. Retinal atrophy has not been found in mice, dogs, monkeys or humans. Mechanistic studies have indicated that the effect is specific to species dependent on hepatic synthesis of the amino acid taurine, which has a protective effect on the retina. Lansoprazole inhibits hepatic synthesis of taurine, however, humans obtain their taurine requirements from the diet.

Hepatic Impairment

Pharmacokinetic studies showed increased exposure in patients with hepatic impairment (see section 5.2). Lansoprazole should only be used where the benefits are considered to outweigh the potential risks.

Dose adjustment is recommended in patients with moderate to severe hepatic impairment (see section 4.2), and patients should be monitored for adverse effects (see section 4.8).

Use in children

The use of LANZOL RELIEF is not recommended in children as clinical data are limited. Treatment of small children below one year of age should be avoided as available data have not shown beneficial effects in the treatment of gastro-oesophageal reflux disease.

Elderly

Dosage adjustment is not required in the elderly.

Effects on Laboratory Tests

Increased Chromogranin A (CgA) level may interfere with investigations for neuroendocrine tumours. To avoid this interference, proton pump inhibitor treatment should be stopped 14 days before CgA measurements.

Other precautions

Agents that elevate gastric pH may increase the already-present risk of nosocomial pneumonia in intubated ICU patients receiving mechanical ventilation.

This medicinal product contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicinal product.

This medicinal product contains Phenylalanine. Phenylalanine may be harmful if you have phenylketonuria (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly.

This medicinal product contains sulfites. May rarely cause severe hypersensitivity reactions and bronchospasm.

4.5 Interaction with other medicines and other forms of interaction

Lansoprazole is metabolised in the liver and is a weak inducer of cytochrome P450. Therefore, there is the possibility of interaction with other medicines metabolised via this system e.g. theophylline,

phenytoin, carbamazepine and warfarin. Patients receiving such medicines concomitantly with lansoprazole should be monitored to determine if any dosage adjustment is necessary.

Tacrolimus

Concomitant administration of lansoprazole and tacrolimus may increase whole blood levels of tacrolimus, especially in transplant patients who are intermediate or poor metabolisers of CYP2C19. Inhibitors of CYP2C19 such as fluvoxamine would likely increase the systemic exposure of lansoprazole. Inducers of CYP2C19 would likely decrease the systemic exposure to lansoprazole.

Sucralfate/Antacids

Sucralfate and antacids may decrease the bioavailability of lansoprazole. Therefore, lansoprazole should be taken at least 1 hour after these medicinal products.

Ketoconazole and Itraconazole

Lansoprazole causes a profound and long-lasting inhibition of gastric acid secretion; therefore, lansoprazole may interfere with the absorption of medicines where gastric pH is an important determinant of bioavailability (e.g. ketoconazole, itraconazole, ampicillin esters, iron salts, digoxin).

Digoxin

Co-administration lansoprazole and digoxin may result in an increase in digoxin plasma levels. Digoxin plasma levels should therefore be monitored, and the digoxin dose adjusted as needed at the start and end of treatment with lansoprazole.

Methotrexate

Concomitant use with methotrexate (primarily at high dose), may elevate and prolong serum levels of methotrexate and/or its metabolite, possible leading to methotrexate toxicities.

HIV Protease Inhibitors

Co-administration is not recommended with HIV protease inhibitors for which absorption is dependent on acidic gastric pH, such as atazanavir and nelfinavir, due to substantial reduction in plasma concentrations of the protease inhibitor.

Other Medication Interactions

No clinically significant effects on plasma levels of warfarin, phenytoin (single IV doses only) and diazepam have been found.

The possibility of interaction between lansoprazole and low dose oral contraceptives cannot be excluded.

There is no evidence of an interaction between lansoprazole and non-steroidal anti-inflammatory drugs (NSAIDs).

4.6 Fertility, pregnancy and lactation

Pregnancy

Pregnancy category B3

Lansoprazole has been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human foetus having been observed. Lansoprazole should not be used during pregnancy unless the benefit outweighs the potential risk to the foetus.

Breastfeeding

Animal studies indicate that lansoprazole is secreted into breast milk. There is no information on the secretion of lansoprazole into breast milk in humans. The use of lansoprazole during breastfeeding should be avoided unless the benefit outweighs the potential risk to the child.

Fertility

No data on the effect of lansoprazole on human fertility are available. For pre-clinical animal data refer to section 5.3.

4.7 Effects on ability to drive and use machines

The occurrence of adverse reactions such as dizziness, vision blurred, or headache may influence the ability to drive and use machinery.

4.8 Undesirable effects

Adverse reactions reported by system organ class and by frequency. Frequencies are defined as: common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1000), very rare (< 1/10,000) and not known (frequency cannot be estimated from the available data).

System Organ Class	Common	Uncommon	Rare	Very Rare	Not Known
Nervous System Disorders	Headache, dizziness		Vertigo, paraesthesia		
Psychiatric Disorder		Depression	Hallucination, confusion		
Gastrointestinal Disorders	Nausea, diarrhoea, abdominal pain, constipation, vomiting, flatulence, dry mouth or throat		Taste disorder	Colitis	Dyspepsia
Hepatobiliary Disorders	Increase in hepatic enzyme levels		Hepatitis, jaundice		
Skin and Subcutaneous Tissue Disorders	Urticaria, pruritus, rash		Petechiae, purpura, diffuse alopecia, erythema multiforme, photosensitivity reaction	Stevens-Johnson syndrome, toxic epidermal necrolysis (Lyell syndrome)	Subacute cutaneous lupus erythematosus, hair thinning

System Organ Class	Common	Uncommon	Rare	Very Rare	Not Known
Immune System Disorders			Angioedema	Anaphylactic Shock	Upper Respiratory Tract Infection
Renal and Urinary Disorders			Tubulointerstitial nephritis		Urinary Tract Infections
Metabolism and Nutrition Disorders					Hyponatraemia, hypomagnesaemia hypocalcaemia and hypokalaemia. Severe hypomagnesaemia may result in hypocalcaemia. Hypomagnesaemia may also result in hypokalaemia (see section 4.4).
Blood and Lymphatic System Disorder		Thrombocytopenia, eosinophilia, leukopenia	Petechiae, purpura		Agranulocytosis, pancytopenia, neutropenia
Musculoskeletal and Connective Tissue Disorders		Arthralgia, myalgia, fracture of the hip, wrist or spine			
Eye Disorders			Vision blurred		
Reproductive System and Breast Disorders			Gynaecomastia, erectile dysfunction		
General Disorders and Administration Site Conditions	Fatigue	Oedema			Wheezing, bruising

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions https://pophealth.my.site.com/carmreportnz/s/.

4.9 Overdose

There is no information on the effect of acute over dosage. In case of overdose, supportive and symptomatic therapy should be initiated.

Doses of up to 180 mg/day for more than a year have been used to treat Zollinger Ellison Syndrome with no serious adverse effects.

For further advice on management of overdose please contact the National Poisons Information Centre (0800 POISON or 0800 764 766).

5. Pharmacological Properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Medicines for peptic ulcer and gastro-oesophageal reflux disease (GORD), ATC code: A02BC03

Mechanism of action

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 in the parietal cells of the stomach. The inhibition is reversible and dose dependent. Its effects extend to both basal and stimulated secretions of gastric acid. Lansoprazole is concentrated in the parietal cells, becomes active in their acidic environment and reacts with the sulphur group of H+/K+ ATPase resulting in inhibition of the enzyme activity.

A single dose of 30 mg lansoprazole inhibits stimulated acid secretion by approximately 80%. Basal acid secretion and basal and stimulated secretion volumes are affected to a lesser degree.

After repeated dosing (for 7 days) 90% inhibition of stimulated acid secretion is achieved. Despite its short elimination half-life, lansoprazole has a prolonged pharmacological action, providing effective suppression of gastric acid secretion over 24 hours.

When used in combination with the recommended antibiotics, it is associated with *H. pylori* eradication rates of up to 90%.

Clinical efficacy and safety

Helicobacter Pylori

In clinical trials, the recommended dosage regimens were associated with *H. Pylori* eradication rates of up to 90%. The best eradication rates were obtained with regimens which included clarithromycin. Trials, which used Lansoprazole 30 mg capsules in combination with only one antibiotic, resulted in significantly lower eradication rates. Therefore, such regimens are not recommended.

Reflux oesophagitis

In two double-blind, placebo controlled multicentre studies (of 336 patients) examining the efficacy of lansoprazole 15 mg and 30 mg tablets in maintaining healed erosive reflux oesophagitis, lansoprazole was significantly superior to placebo in maintaining endoscopic and symptomatic freedom from disease. The time to median recurrence of either symptoms or endoscopic evidence of disease was less than 1 month for the placebo and greater then 12 months for 15 mg and 30 mg lansoprazole ($p \leq 0.001$). There was a slight trend for a better outcome with 30 mg lansoprazole although this was not statistically significant.

A study in 266 patients comparing lansoprazole 15 mg and 30 mg daily with ranitidine 300 mg twice daily, found both lansoprazole 15 mg and 30 mg increased the time to relapse and probability of no relapse in comparison to ranitidine. The percentage of patients who relapsed endoscopically during the 12-month maintenance period was 31% in the lansoprazole 15 mg group, 20% in the

lansoprazole 30 mg group and 68% in the ranitidine group. The difference between the lansoprazole groups and the ranitidine was apparent from the earliest time point in the study and maintained throughout the 12-month period. Comparison of treatment groups with regard to symptom control showed similar superiority of lansoprazole over ranitidine ($p \leq 0.001$ for each comparison).

A study in 882 patients comparing lansoprazole 15 mg and 30 mg daily with omeprazole 20 mg daily showed endoscopic remission rates (after 12 months) of 75% with lansoprazole 15 mg daily, 88% with lansoprazole 30 mg daily and 89% with omeprazole 20 mg daily. The results demonstrate that lansoprazole 30 mg daily achieved significantly better remission rates compared to lansoprazole 15 mg daily and is of equal efficacy to omeprazole 20 mg daily.

The results of the 4 pivotal studies examining the use of lansoprazole in the long-term management of reflux oesophagitis are tabulated below:

Endoscopically proven relapse rates at 12 months

Study	Lansoprazole 15 mg l.d.	Lansoprazole 30 mg l.d.	Ranitidine 300 mg b.d.	Omeprazole 20 mg l.d.	Placebo
1 (n=163)	37%	39%	-	-	92%
2 (n=184)	13%	11%	-	-	
3 (n=569)	31%	20%	68%*	-	
4 (n=882)	25%	12%	-	11%	

- not included in the study
* ($p \leq 0.001$) versus lansoprazole 15 mg and 30 mg
# ($p \leq 0.001$) versus omeprazole 20 mg and lansoprazole 30 mg

Duodenal ulcer

In a study comparing lansoprazole 15 mg daily with placebo in 180 patients with endoscopically documented duodenal ulcer, the percentage of patients who remained healed after twelve months was significantly higher with lansoprazole than with placebo. Lansoprazole 15 mg was significantly superior to placebo in preventing endoscopic and symptomatic relapses of disease.

Duodenal ulcer recurrence rates						
Treatment	Interval (months)					
	0-1	1-2	2-3	3-6	6-9	9-12
Placebo	20%	36%	52%	60%	60%	62%
Lansoprazole 15 mg	2%*	8%*	10%*	14%*	15%*	17%*

*($p < 0.001$) versus placebo

The maintenance studies discussed, using lansoprazole 15 mg and 30 mg did not extend beyond 12 months.

5.2 Pharmacokinetic properties

Absorption

Lansoprazole is well absorbed and exhibits high bioavailability (80-90%) following an oral dose. Peak plasma levels occur within 1.5 to 2.0 hours. The bioavailability has been shown to be affected by the presence of food, however, acid inhibition (which is an endpoint for efficacy), as measured from sampling of gastric juice in healthy volunteers, is not significantly affected by food. It was shown in one study that morning dosing produced higher mean gastric pH values than afternoon dosing.

Distribution

Plasma protein binding is high (97%) and is gender and concentration independent. Binding does not change as a result of multiple dosing.

After IV administration, the volume of distribution is 29 ± 4 L, total clearance is 31 ± 8 L/h and elimination half-life is 0.9 ± 0.44 hours.

Elimination

Following absorption, lansoprazole is primarily metabolised by the liver and the metabolites are excreted by both the renal and biliary route. A study with ^{14}C-labelled lansoprazole showed that up to 50% of the label was excreted in the urine, although unchanged medicine does not appear to be excreted by this route; unchanged medicine is eliminated, however, by biliary excretion. The plasma elimination half-life in healthy subjects ranges from 1 to 2 hours following a single dose or multiple doses. In patients with various degrees of chronic hepatic impairment, the mean plasma half-life of lansoprazole was prolonged from 1.5 hours to 3.2 to 7.2 hours. The exposure of lansoprazole is doubled in patients with mild hepatic impairment and much more increased in patients with moderate and severe hepatic impairment.

5.3 Preclinical safety data

Fertility

Reproductive studies conducted in pregnant rats and rabbits at oral doses up to 300 and 30 mg/kg/day, respectively, did not disclose any evidence of a teratogenic effect. A significant increase in foetal mortality was observed in the rabbit study at doses above 10 mg/kg/day. In rats a slight reduction in litter survival and weights was noted at doses above 100 mg/kg/day.

The effects of lansoprazole on human male fertility have not been evaluated.

Carcinogenicity

In a 2 year carcinogenicity study in rats, oral doses of 5, 15 or 50 mg/kg/day, 5 days per week produced gastric ECL cell hyperplasia and carcinoid tumours in a dose-related manner in both male and female rats. The incidence of these effects was markedly higher in female rats. A “no effect” dose was not established for female rats. An increased incidence of benign Leydig cell tumours and testicular hyperplasia was also reported at dose levels of 15 mg/kg/day. Two repeat 2 year carcinogenicity studies in rats using doses ranging from 5-150 mg/kg/day, 7 days per week confirmed these findings.

In mice, a 78 week carcinogenicity study was performed at doses of 1.5, 5, 15 and 50 mg/kg/day, 5 days per week. No gastric ECL cell carcinoids were seen. In a repeat carcinogenicity study, mice were dosed with 15, 75, 150 or 300 mg/kg/day, 7 days a week. Terminal studies showed ECL cell hyperplasia, mucosal hyperplasia/hypertrophy and glandular dilatation and vacuolation at all dosages. Carcinoids were found in occasional animals receiving 15, 150 or 300 mg/kg/day.

Hypergastrinaemia secondary to prolonged hypochlorhydria has been postulated to be the mechanism by which ECL cell hyperplasia and gastric carcinoid tumours develop.

Mutagencity

Negative results were obtained in gene mutation assays and in an *in vivo* assay of chromosomal damage. *In vitro* assays of chromosomal damage showed evidence of chromosomal aberrations, though this may reflect cytotoxicity rather than genotoxic activity.

6. Pharmaceutical Particulars

6.1 List of excipients

LANZOL RELIEF capsules also contains:

- sugar spheres,
- heavy magnesium carbonate,
- sucrose,
- corn starch,
- hydroxypropyl cellulose,
- methacrylic acid-ethyl acetate copolymer,
- talc,
- polyethylene glycol,
- titanium dioxide,
- polysorbate 80
- colloidal anhydrous silica.

The hard gelatin capsules also contains:

- gelatin
- titanium dioxide and
- are imprinted with Tek Print Ink SW-9009.

Additionally the 15 mg gelatin capsules contain the following permitted colourants, FD & C Green # 3 and FD & C Red # 40 and the 30 mg gelatin capsules FD & C Blue # 1 and FD & C Red # 3.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store at or below 25°C.

6.5 Nature and contents of container

15 mg capsules are available in blister packs containing 28 or 30 capsules, or bottles containing 30, 100, 500, 1000 capsules.

30 mg capsules are available in blister packs containing 28 or 30 capsules, or bottles containing 30, 100, 500, 1000 capsules.

Not all pack types and sizes may be marketed.

6.6 Special precautions for disposal

Not applicable.

7. Medicines Schedule

Prescription Medicine

8. Sponsor Details

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AUCKLAND
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Telephone 0800 168 169

9. Date of First Approval

17 June 2010

10. Date of Revision of the Text

08 January 2024

Summary table of changes

Section	**Summary of new information**
2	Updated excipients with known effect Addition of allergen declaration
4.1	Addition of new indication Removal of United States National Institute of Health information
4.1, 4.3	Minor formatting update
4.2	Updated dose recommendation in patients with moderate or severe hepatic impairment
4.3	Removal of severe hepatic impairment as a contraindication
4.4	Addition of information on the influence of lansoprazole on vitamin B12 absorption and effects on laboratory test results. Updated information on hypomagnesaemia, risk of fractures and SCLE Addition of information in use in hepatic impairment.
4.4, 4.5, 4.6, 4.7, 5.1, 5.2	Minor editorial changes
4.5	Addition of interaction with tacrolimus, sucralfate, antacids, itraconazole, digoxin and HIV Protease inhibitors. Updated information on interactions with methotrexate
4.6	Updated information on use in pregnancy
4.7	Updated information of ability to drive and use machines
4.8	Updated adverse reactions information including frequency of ADR reports Updated ADR reporting website
5.1	Updated mechanism of action information
5.2	Updated pharmacokinetic information in patients with hepatic impairment
6.1	Removal of allergen declaration