

# Summary of Product Characteristics

## 1 NAME OF THE MEDICINAL PRODUCT

Pantium 40mg Gastro-Resistant Tablets

## 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gastro-resistant tablet contains:

40 mg of pantoprazole (equivalent to 45.1 mg pantoprazole sodium sesquihydrate)

### Excipients with known effect

Each gastro-resistant tablet contains 76.85 mg maltitol, 0.690 mg lecithin (derived from soya oil) and 3.68 mg sodium (see section 4.4).

For the full list of excipients, see section 6.1.

## 3 PHARMACEUTICAL FORM

Gastro-resistant tablet

Yellow, oval tablet.

## 4 CLINICAL PARTICULARS

### 4.1 Therapeutic Indications

- Combination therapy with two suitable antibiotics for the eradication of *Helicobacter pylori* and for the prevention of relapse of peptic ulcers in patients with *Helicobacter pylori* associated ulcers.
- duodenal ulcers.
- gastric ulcers.
- moderate and severe forms of reflux oesophagitis.
- long-term treatment of Zollinger-Ellison syndrome and other disorders accompanied by pathological gastric acid hypersecretion.

### 4.2 Posology and method of administration

#### Posology

*Adults and adolescents 12 years of age and above*

#### Reflux oesophagitis

One tablet of Pantium 40 mg per day.

In individual cases the dose may be doubled (increase to 2 tablets pantoprazole daily) especially when there has been no response to other treatment. A 4 week period is usually required for the treatment of reflux oesophagitis. If this is not sufficient, healing will usually be achieved within a further 4 weeks.

#### *Adults*

#### Eradication of *H. pylori* in combination with two appropriate antibiotics

In *H. pylori*-positive patients with gastric and duodenal ulcers, eradication of the germ by a combination therapy should be achieved. Considerations should be given to official local guidance (e.g. national recommendations) regarding bacterial resistance and the appropriate use and prescription of antibacterial agents. Depending upon the resistance pattern, the following combinations can be recommended for the eradication of *H. pylori*:

- a) twice daily one tablet Pantium 40 mg  
+ twice daily 1,000 mg amoxicillin  
+ twice daily 500 mg clarithromycin

- b) twice daily one tablet Pantium 40 mg
  - + twice daily 400 - 500 mg metronidazole (or 500 mg tinidazole)
  - + twice daily 250 - 500 mg clarithromycin
- c) twice daily one tablet Pantium 40 mg
  - + twice daily 1,000 mg amoxicillin
  - + twice daily 400 - 500 mg metronidazole (or 500 mg tinidazole)

In combination therapy for eradication of *H. pylori* infection, the second pantoprazole tablet should be taken 1 hour before the evening meal. The combination therapy is implemented for 7 days in general and can be prolonged for a further 7 days to a total duration of up to two weeks. If, to ensure healing of the ulcers, further treatment with pantoprazole is indicated, the dose recommendations for duodenal and gastric ulcers should be considered.

If combination therapy is not an option, e.g. if the patient has tested negative for *H. pylori*, the following dose guidelines apply for pantoprazole monotherapy:

#### Treatment of gastric ulcer

One tablet of Pantium 40 mg per day. In individual cases the dose may be doubled (increase to 2 tablets of Pantium 40 mg daily) especially when there has been no response to other treatment. A 4 week period is usually required for the treatment of gastric ulcers. If this is not sufficient, healing will usually be achieved within a further 4 weeks.

#### Treatment of duodenal ulcer

One tablet of Pantium 40 mg per day. In individual cases the dose may be doubled (increase to 2 tablets of Pantium 40 mg daily) especially when there has been no response to other treatment. A duodenal ulcer generally heals within 2 weeks. If a 2-week period of treatment is not sufficient, healing will be achieved in almost all cases within a further 2 weeks.

#### Zollinger-Ellison syndrome and other pathological hypersecretory conditions

For the long-term management of Zollinger-Ellison syndrome and other pathological hypersecretory conditions patients should start their treatment with a daily dose of 80 mg (2 tablets of Pantium 40 mg). Thereafter, the dose can be titrated up or down as needed using measurements of gastric acid secretion to guide. With doses above 80 mg daily, the dose should be divided and given twice daily. A temporary increase of the dose above 160 mg pantoprazole is possible but should not be applied longer than required for adequate acid control.

Treatment duration in Zollinger-Ellison syndrome and other pathological hypersecretory conditions is not limited and should be adapted according to clinical needs

#### *Patients with hepatic impairment*

A daily dose of 20 mg pantoprazole (1 tablet of 20 mg pantoprazole) should not be exceeded in patients with severe liver impairment. Pantoprazole must not be used in combination treatment for eradication of *H. pylori* in patients with moderate to severe hepatic dysfunction since currently no data are available on the efficacy and safety of pantoprazole in combination treatment of these patients (see section 4.4).

#### *Patients with renal impairment*

No dosage adjustment is necessary in patients with impaired renal function. Pantoprazole must not be used in combination treatment for eradication of *H. pylori* in patients with impaired renal function since currently no data are available on the efficacy and safety of pantoprazole in combination treatment for these patients (see section 5.2)..

#### *Older people*

No dose adjustment is necessary in older people (see section 5.2).

#### *Paediatric population*

Pantoprazol is not recommended for use in children below 12 years of age because of limited data on safety and efficacy in the age group (see section 5.2).

#### Method of administration

##### Oral use

The tablets should not be chewed or crushed, and should be swallowed whole 1 hour before a meal with some water.

### 4.3 Contraindications

Hypersensitivity to the active substance, substituted benzimidazoles, any of the excipients listed in section 6.1.

Pantium 40 mg contains soya lecithin and must not be used in patients who are hypersensitive to peanut or soya.

### 4.4 Special warnings and precautions for use

#### *Hepatic impairment*

In patients with severe liver impairment, the liver enzymes should be monitored regularly during treatment with pantoprazole, particularly on long-term use. In the case of a rise of the liver enzymes, the treatment should be discontinued (see section 4.2).

#### *Combination therapy*

In the case of combination therapy, the summaries of product characteristics of the respective medicinal products should be observed.

#### *Gastric malignancy*

Symptomatic response to pantoprazole may mask the symptoms of gastric malignancy and may delay diagnosis. In the presence of any alarm symptom (e. g. significant unintentional weight loss, recurrent vomiting, dysphagia, haematemesis, anaemia or melaena) and when gastric ulcer is suspected or present, malignancy should be excluded.

Further investigation is to be considered if symptoms persist despite adequate treatment.

#### *Co-administration with HIV protease inhibitors*

Co-administration of pantoprazole is not recommended with HIV protease inhibitors for which absorption is dependent on acidic intragastric pH such as atazanavir, due to significant reduction in their bioavailability (see section 4.5).

#### *Influence on vitamin B12 absorption*

In patients with Zollinger-Ellison syndrome and other pathological hypersecretory conditions requiring long-term treatment, pantoprazole, as all acid-blocking medicines, may reduce the absorption of vitamin B12 (cyanocobalamin) due to hypo- or achlorhydria. This should be considered in patients with reduced body stores or risk factors for reduced vitamin B12 absorption on long-term therapy or if respective clinical symptoms are observed.

#### *Long term treatment*

In long-term treatment, especially when exceeding a treatment period of 1 year, patients should be kept under regular surveillance.

#### *Gastrointestinal infections caused by bacteria*

Pantoprazole, like all proton pump inhibitors (PPIs), might be expected to increase the counts of bacteria normally present in the upper gastrointestinal tract. Treatment with pantoprazole may lead to a slightly increased risk of gastrointestinal infections caused by bacteria such as *Salmonella* and *Campylobacter* and *C. difficile*.

#### *Hypomagnesaemia*

Severe hypomagnesaemia has been reported in patients treated with PPIs like pantoprazole for at least three months, and in most cases for a year. Serious manifestations of hypomagnesaemia such as fatigue, tetany, delirium, convulsions, dizziness and ventricular arrhythmia can occur but they may begin insidiously and be overlooked. In most affected patients, hypomagnesaemia improved after magnesium replacement and discontinuation of the PPI.

For patients expected to be on prolonged treatment or who take PPIs with digoxin or medicinal products that may cause hypomagnesaemia (e.g., diuretics), health care professionals should consider measuring magnesium levels before starting PPI treatment and periodically during treatment.

#### *Bone fractures*

Proton pump inhibitors, especially if used in high doses and over long durations (> 1 year), may modestly increase the risk of hip, wrist and spine fracture, predominantly 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 health care professional should consider stopping pantoprazole. SCLE after previous treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.

#### Excipients

This medicinal product contains maltitol. Patients with rare hereditary problems of fructose intolerance should not take this medicinal product.

This medicinal product contains less than 1 mmol sodium (23 mg) per gastro-resistant tablet, that is to say essentially 'sodium-free'.

### **4.5 Interaction with other medicinal products and other forms of interactions**

#### Medicinal products with pH-dependent absorption pharmacokinetics

Because of profound and long lasting inhibition of gastric acid secretion, pantoprazole may interfere with the absorption of other medicinal products where gastric pH is an important determinant of oral availability, e.g. some azole antifungals such as ketoconazole, itraconazole, posaconazole and other medicines such as erlotinib.

#### HIV protease inhibitors

Co-administration of pantoprazole is not recommended with HIV protease inhibitors for which absorption is dependent on acidic intragastric pH such as atazanavir due to significant reduction in their bioavailability (see section 4.4).

If the combination of HIV protease inhibitors with a proton pump inhibitor is judged unavoidable, close clinical monitoring (e.g. virus load) is recommended. A pantoprazole dose of 20 mg per day should not be exceeded. Dosage of the HIV protease inhibitor may need to be adjusted.

#### Coumarin anticoagulants (phenprocoumon or warfarin)

Co-administration of pantoprazole with warfarin or phenprocoumon did not affect the pharmacokinetics of warfarin, phenprocoumon or INR. However, there have been reports of increased INR and prothrombin time in patients receiving PPIs and warfarin or phenprocoumon concomitantly. Increases in INR and prothrombin time may lead to abnormal bleeding, and even death. Patients treated with pantoprazole and warfarin or phenprocoumon may need to be monitored for increase in INR and prothrombin time.

#### Methotrexate

Concomitant use of high dose methotrexate (e.g. 300 mg) and proton-pump inhibitors has been reported to increase methotrexate levels in some patients. Therefore in settings where high-dose methotrexate is used, for example cancer and psoriasis, a temporary withdrawal of pantoprazole may need to be considered.

#### Other interactions studies

Pantoprazole is extensively metabolised in the liver via the cytochrome P450 enzyme system. The main metabolic pathway is demethylation by CYP2C19 and other metabolic pathways include oxidation by CYP3A4.

Interaction studies with medicinal products also metabolised with these pathways, like carbamazepine, diazepam, glibenclamide, nifedipine, and an oral contraceptive containing levonorgestrel and ethinyl oestradiol, did not reveal clinically significant interactions.

An interaction of pantoprazole with other medicinal products or compounds, which are metabolised using the same enzyme system, cannot be excluded.

Results from a range of interaction studies demonstrate that pantoprazole does not affect the metabolism of active substances metabolised by CYP1A2 (such as caffeine, theophylline), CYP2C9 (such as piroxicam, diclofenac, naproxen), CYP2D6 (such as metoprolol), CYP2E1 (such as ethanol), or does not interfere with p-glycoprotein related absorption of digoxin.

There were no interactions with concomitantly administered antacids.

Interaction studies have also been performed by concomitantly administering pantoprazole with the respective antibiotics (clarithromycin, metronidazole, amoxicillin). No clinically relevant interactions were found.

Medicinal products that inhibit or induce CYP2C19:

Inhibitors of CYP2C19 such as fluvoxamine could increase the systemic exposure of pantoprazole. A dose reduction may be considered for patients treated long-term with high doses of pantoprazole, or those with hepatic impairment.

Enzyme inducers affecting CYP2C19 and CYP3A4 such as rifampicin and St John's wort (*Hypericum perforatum*) may reduce the plasma concentrations of PPIs that are metabolised through these enzyme systems.

#### 4.6 Fertility, pregnancy and lactation

##### Pregnancy

A moderate amount of data on pregnant women (between 300-1,000 pregnancy outcomes) indicate no malformative or foeto/neonatal toxicity of pantoprazole.

Animal studies have shown reproductive toxicity (see section 5.3).

As a precautionary measure, it is preferable to avoid the use of pantoprazole during pregnancy.

##### Breastfeeding

Animal studies have shown excretion of pantoprazole in breast milk. There is insufficient information on the excretion of pantoprazole in human milk but excretion into human milk has been reported. A risk to the newborns/infants cannot be excluded. Therefore, a decision on whether to discontinue breastfeeding or to discontinue/abstain from pantoprazole therapy should take into account the benefit of breastfeeding to the child, and the benefit of pantoprazole therapy for the woman.

##### Fertility

There was no evidence of impaired fertility following the administration of pantoprazole in animal studies (see section 5.3).

#### 4.7 Effects on ability to drive and use machines

Pantoprazole has no or negligible influence on the ability to drive and use machines.

Adverse drug reactions, such as dizziness and visual disturbances may occur (see section 4.8). If affected, patients should not drive or operate machines.

#### 4.8 Undesirable effects

Approximately 5 % of patients can be expected to experience adverse drug reactions (ADRs). The most commonly reported ADRs are diarrhoea and headache, both occurring in approximately 1 % of patients.

The table below lists adverse reactions reported with pantoprazole, ranked under the following frequency classification: Very common ( $\geq 1/10$ ); common ( $\geq 1/100$  to  $< 1/10$ ); uncommon ( $\geq 1/1,000$  to  $< 1/100$ ); rare ( $\geq 1/10,000$  to  $< 1/1,000$ ); very rare ( $< 1/10,000$ ), not known (cannot be estimated from the available data).

For all adverse reactions reported from post-marketing experience, it is not possible to apply any Adverse Reaction frequency and therefore they are mentioned with a "not known" frequency.

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

Table 1. Adverse reactions with pantoprazole in clinical trials and post-marketing experience

<b>Frequency</b>	<b>Common</b>	<b>Uncommon</b>	<b>Rare</b>	<b>Very rare</b>	<b>Not known</b>
<b>System organ class</b>					
<b>Blood and lymphatic system disorders</b>			Agranulocytosis	Leukopenia, thrombocytopenia, pancytopenia	
<b>Immune system disorders</b>			Hypersensitivity (including anaphylactic reactions and anaphylactic shock)		
<b>Metabolism and nutrition disorders</b>			Hyperlipidaemias and lipid increases (triglycerides, cholesterol), Weight changes		Hyponatraemia, Hypomagnesaemia (see section 4.4), Hypocalcaemia <sup>(1)</sup> ,

<b>Frequency</b>	<b>Common</b>	<b>Uncommon</b>	<b>Rare</b>	<b>Very rare</b>	<b>Not known</b>
<b>System organ class</b>					Hypokalaemia
<b>Psychiatric disorders</b>		Sleep disorders	Depression (and all aggravations)	Disorientation (and all aggravations)	Hallucination, Confusion (especially in predisposed patients as well as the aggravation of these symptoms in case of pre-existence)
<b>Nervous system disorders</b>		Headache, Dizziness	Taste disorders		Paraesthesia
<b>Eye disorders</b>			Disturbances in vision / blurred vision		
<b>Gastro-intestinal disorders</b>	Fundic gland polyps (Benign)	Diarrhoea, Nausea/ vomiting, Abdominal distension and bloating, Constipation, Dry mouth, Abdominal pain and discomfort			Microscopic colitis
<b>Hepato-biliary disorders</b>		Liver enzymes increased (transaminases, $\gamma$ -GT)	Bilirubin increased		Hepatocellular injury, Jaundice, Hepatocellular failure
<b>Skin and sub-cutaneous tissue disorders</b>		Rash / exanthema / eruption, Pruritus	Urticaria, Angioedema		Stevens Johnson syndrome, Lyell syndrome, Erythema multiforme, Photosensitivity, Subacute cutaneous lupus erythematosus (see section 4.4)
<b>Musculo-skeletal, connective tissue disorders</b>		Fracture of the hip, wrist or spine (see section 4.4)	Arthralgia, Myalgia		Muscle spasm <sup>(2)</sup>
<b>Renal and urinary disorders</b>					Interstitial nephritis (with possible progression to renal failure)
<b>Reproductive system and breast disorders</b>			Gynaecomastia		
<b>General disorders and</b>		Asthenia, Fatigue and	Body temperature increased, Oedema peripheral		

<b>Frequency</b>	<b>Common</b>	<b>Uncommon</b>	<b>Rare</b>	<b>Very rare</b>	<b>Not known</b>
<b>System organ class</b>					
<b>administration site conditions</b>		malaise			

<sup>(1)</sup> Hypocalcaemia in association with hypomagnesaemia

<sup>(2)</sup> Muscle spasm as a consequence of electrolyte disturbance

#### 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 HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

## 4.9 Overdose

There are no known symptoms of overdose in man.

Systemic exposure with up to 240 mg administered intravenously over 2 minutes, were well tolerated.

As pantoprazole is extensively protein bound, it is not readily dialysable.

In the case of an overdose with clinical signs of intoxication, apart from symptomatic and supportive treatment, no specific therapeutic recommendations can be made.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: proton pump inhibitors

ATC code: A02B C02

Pantoprazole is a substituted benzimidazole which inhibits gastric acid secretion by specifically reacting with the proton pumps of parietal cells.

Pantoprazole is converted to its active form in the acidic channel of the parietal cells where it inhibits the H<sup>+</sup>/K<sup>+</sup>-ATPase enzyme, i.e. the final stage in the production of hydrochloric acid in the stomach. The inhibition is dose-dependent and affects both basal and stimulated acid secretion. In most patients, freedom from symptoms is achieved in 2 weeks. As with other proton pump inhibitors and H<sub>2</sub> receptor inhibitors, treatment with pantoprazole causes a reduced acidity in stomach and thereby an increase in gastrin in proportion to the reduction in acidity. The increase in gastrin is reversible. Since pantoprazole binds to the enzyme distal to the cell receptor level, the substance can affect hydrochloric acid secretion independently of stimulation by other substances (acetylcholine, histamine, gastrin). The effect is the same whether the product is administered orally or intravenously.

The fasting gastrin values increase under pantoprazole. On short-term use, in most cases they do not exceed the normal upper limit. During long-term treatment, gastrin levels double in most cases. An excessive increase, however, occurs only in isolated cases. As a result, a mild to moderate increase in the number of specific endocrine (ECL) cells in the stomach is observed in a minority of cases during long-term treatment (simple to adenomatoid hyperplasia). However, according to the studies conducted so far (see section 5.3), the formation of carcinoid precursors (atypical hyperplasia) or gastric carcinoids can be ruled out for humans.

An influence of a long term treatment with pantoprazole exceeding one year cannot be completely ruled out on endocrine parameters of the thyroid and liver enzymes according to results in animal studies.

During treatment with antisecretory medicinal products, serum gastrin increases in response to the decreased acid secretion. Also CgA increases due to decreased gastric acidity. The increased CgA level may interfere with investigations for neuroendocrine tumours. Available published evidence suggests that proton pump inhibitors should be discontinued between 5 days and 2 weeks prior to CgA measurements. This is to allow CgA levels that might be spuriously elevated following PPI treatment to return to reference range.

### 5.2 Pharmacokinetic properties

#### General pharmacokinetics

Pantoprazole is rapidly absorbed. Even after a single oral dose of 20 mg pantoprazole, maximum concentrations of the active substance are achieved. On average, peak serum concentrations of 1 – 1.5 µg/ml approx. are reached within 2 hours post-dose, and remain constant even after multiple dosing. Volume of distribution is 0.15 l/kg approx. and clearance is approximately 0.1 l/h/kg. Its terminal elimination half-life was calculated to be 1 hour approx. A few cases of subjects with delayed elimination have been observed. Due to the specific activity of pantoprazole within the parietal cell, there is no correlation between elimination half-life and the much longer duration of action (inhibition of acid secretion).

There is no variation in pharmacokinetic characteristics after single or repeated dosing. Within the dose range of 10-80 mg, the kinetics of pantoprazole is virtually linear, both after oral and intravenous dosing.

Serum protein binding of pantoprazole is around 98 %. Pantoprazole is almost exclusively metabolised by the liver. Most of its metabolites (80 % approx.) are renally excreted; the remainder are excreted with the faeces. In both serum and urine, the main metabolite is desmethylpantoprazole which is conjugated with sulphate. Half-life of the main metabolite (about 1.5 hours) is not significantly longer than that of pantoprazole.

#### Bioavailability

Pantoprazole is completely absorbed after oral dosing. Absolute bioavailability of the tablet was found to be about 77 %. Concomitant intake of food or antacids had no influence on AUC, maximum serum concentrations and thus bioavailability. Administration with food may delay its absorption up to 2 h or longer.

#### Special patient groups

No dose reduction is required when pantoprazole is administered to patients with impaired renal function (including patients on dialysis). As with healthy subjects, the half-life of pantoprazole is short. Only very small amounts of pantoprazole are dialysed. Although the main metabolite has a moderately prolonged half-life (2 – 3 hours), excretion is nevertheless rapid and thus accumulation does not occur.

In patients with liver cirrhosis (classes A and B according to Child), its half-life is prolonged to values ranging from 7 to 9 hours, and AUC values are increased by a factor of 5-7. Compared with healthy subjects, peak serum concentrations increase only slightly by a factor of 1.5.

Similarly, the slight increase in AUC and  $C_{max}$  in elderly subjects compared with younger counterparts has no clinical relevance.

#### Paediatric population

Following administration of single oral doses of 20 or 40 mg pantoprazole to children aged 5-16 years AUC and  $C_{max}$  were in the range of corresponding values in adults.

Following administration of single IV doses of 0.8 or 1.6 mg/kg pantoprazole to children aged 2-16 years there was no significant association between pantoprazole clearance and age or weight. AUC and volume of distribution were in accordance with data from adults.

### **5.3 Preclinical safety data**

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity and genotoxicity.

In the 2-year carcinogenicity study in rats, neuroendocrine neoplasms were found. In addition, squamous cell papillomas were found in the fore-stomach of rats in one study. The mechanism leading to the formation of gastric carcinoids by substituted benzimidazoles has been carefully investigated and allows the conclusion that it is a secondary reaction to the massively elevated serum gastrin levels occurring in the rat during chronic treatment.

In the two-year rodent studies an increased number of liver tumours was observed in rats (in one rat study only) and in female mice and was interpreted as being due to the high metabolic rate in the liver.

A slight increase in neoplastic changes of the thyroid was observed in the group rats receiving the highest dose (200 mg/kg) in one 2-year study. The occurrence of these neoplasms is associated with pantoprazole-induced changes in the breakdown of thyroxine in the rat liver. As the therapeutic human dose is low, no adverse reactions on the thyroid glands are expected.

Investigations revealed no evidence of impaired fertility or teratogenic effects. Daily doses above 5 mg/kg led to delayed development of the skeleton in rats.

Penetration of the placenta was investigated in the rat and was found to increase with advanced gestation. As a result, concentration of pantoprazole in the foetus is increased shortly before birth.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

#### *Tablet core*

Maltitol (E965)  
Crospovidone type B  
Carmellose Sodium  
Sodium Carbonate, Anhydrous (E500)  
Calcium Stearate

#### *Tablet coating*

Poly(vinyl alcohol)  
Talc (E553b)  
Titanium Dioxide (E171)  
Macrogol 3350  
Soya Lecithin (E322)  
Iron Oxide Yellow (E172)  
Sodium Carbonate, Anhydrous (E500)  
Methacrylic Acid/ethyl acrylate Copolymer (1:1)  
Triethyl Citrate (E1505)

### 6.2 Incompatibilities

Not applicable

### 6.3 Shelf life

For Alu-Alu blisters: 5 years.  
For HDPE bottles: 5 years.

After first opening of the bottle use the medicinal product within three months.

### 6.4 Special precautions for storage

Do not store above 25°C.

### 6.5 Nature and contents of container

Alu-Alu blisters  
HDPE bottles with PP closure and desiccant

#### **Pack sizes:**

7, 14, 15, 28, 30, 56, 60, 100 gastro-resistant tablets (blister packs)

100 gastro-resistant tablets (HDPE bottles)

Not all pack sizes may be marketed.

### 6.6 Special precautions for disposal and other handling

No special requirements.

## 7 MARKETING AUTHORISATION HOLDER

Clonmel Healthcare Ltd  
Clonmel  
Co. Tipperary  
Ireland

**8 MARKETING AUTHORISATION NUMBER**

PA0126/175/002

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

Date of first authorisation: 3<sup>rd</sup> October 2008

Date of last renewal: 20<sup>th</sup> December 2012

**10 DATE OF REVISION OF THE TEXT**

October 2019