SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

PROTECH 40 mg Enteric-Coated Tablet

2. QUALITATIVE AND QUANTITATIVE COMPOSITIONS

Active substance:

Pantoprazole 40 mg (45.10 mg of pantoprazole sodium sesquihydrate)

Excipients:

Anhydrous sodium carbonate	10 mg
Sodium lauryl sulphate	0,13 mg
Sodium bicarbonate	0,28 mg

See section 6.1 for a full list of excipients.

3. PHARMACEUTICAL FORM

Enteric-coated tablets

Yellow, rounded, enteric-coated tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

In adults and adolescents 12 years of age and above:

It is indicated in the treatment of gastroesophageal reflux disease.

In adults:

- In combination with appropriate antibiotics, for the eradication of this microorganism in Helicobacter pylori (H. pylori) -related duodenal and gastric ulcer
- In peptic ulcer (duodenal ulcer and gastric ulcer),
- Zollinger Ellison Syndrome and other pathological hypersecretory conditions.

4.2 Posology and method of administration

Posology / application frequency and duration:

In adults and adolescents 12 years of age and above:

In gastroesophageal reflux disease

One tablet of PROTECH per day is recommended. In individual cases the dose may be doubled (increase to 2 tablets daily). An additional 4 weeks of treatment may be considered for patients not recovering at the end of 4 weeks of treatment.

In adults:

In eradication of H. pylori in combination with two appropriate antibiotics

In H. pylori positive gastric and duodenal ulcer patients, combined treatment should be performed to remove the agent completely. Official local guidelines such as national recommendations should be taken into account for resistance and prescribing appropriate antibiotics. For H. pylori eradication, the following combinations may be proposed depending on the resistance status:

a) twice daily one tablet PROTECH
+ twice daily 1000 mg amoxicillin
+ twice daily 500 mg clarithromycin

b) twice daily one tablet PROTECH
+ twice daily 400 - 500 mg metronidazole (or 500 mg tinidazole)
+ twice daily 250 - 500 mg clarithromycin

c) twice daily one tablet PROTECH
+ twice daily 1000 mg amoxicillin
+ twice daily 500 mg metronidazole (or 500 mg tinidazole)

For combination therapy for H. pylori eradication, the second PROTECH 40 mg Enteric Coated Tablet should be taken 1 hour before dinner.Combination therapy is usually administered for 7 days and can be extended for up to 7 additional days up to a total of 2 weeks.If treatment with pantoprazole for ulcer therapy is to be continued, dose recommendations for duodenal and gastric ulcers should be considered.

In cases where combined treatment is not required, for example if the patient is H.pylori negative, the following dosage of PROTECH 40 mg Enteric Coated Tablet monotherapy is administered:

In treatment of gastric ulcer

One tablet of PROTECH per day is taken. In individual cases the dose may be doubled (increase to 2 tablets PROTECH 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 PROTECH per day. In individual cases the dose may be doubled (increase to 2 tablets PROTECH 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 PROTECH 40 mg). Thereafter, the dosage 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 dosage 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.

Method of Administration:

It is for oral use.

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

Additional Information about Special populations:

Renal Impairment

No dose adjustment is necessary in patients with impaired renal function. PROTECH 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 PROTECH in combination treatment for these patients.

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. PROTECH 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 PROTECH in combination treatment of these patients (See Section 4.4).

Pediatric Population:

Due to limited data on efficacy and safety in children under 12 years of age, PROTECH is not recommended for use in children in this age group (See Section 5.2).

Geriatric Population:

No dose adjustment is necessary in elderly patients (See Section 5.2).

4.3 Contraindications

PROTECH should not be used in patients with known hypersensitivity to the active substance, branched benzimidazoles or any of the excipients listed in Section 6.1.

4.4 Special warnings and special 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 symptoms of gastric malignancy and delay diagnosis. In the presence of any alarm symptoms (eg, unexpected weight loss, recurrent vomiting, dysphagia, hematemesis, anemia, or melena) and in the presence or suspicion of gastric ulcer, the possibility of malignancy should be excluded. If symptoms persist despite appropriate treatment, further investigations should be performed.

Concomitant use with HIV protease inhibitors:

Co-administration of pantoprazole with HIV protease inhibitors whose absorption is dependent on acidic intragastric pH, such as atazanavir, is not recommended due to a 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.

Bone fractures

Several published observational studies suggest that proton pump inhibitor (PPI) therapy may be associated with an increased risk of fracture of the hip, wrist, or osteoporosis in the spine.

Predominantly elderly patients or patients with other known risk factors receiving high doses, defined as multiple daily doses and long-term PPI therapy (one year or more), have an increased risk of fracture. Patients should receive the lowest dose and the shortest duration of PPI therapy for the condition they are treated.

Observational studies reveal that PPIs can increase the overall fracture risk by 10-40%. Some of this increase may be related to other risk factors. Patients at risk for osteoporosis should be treated in accordance with current treatment guidelines and should receive adequate amounts of vitamin D and calcium.

Hypomagnesaemia

Symptomatic and asymptomatic hypomagnesemia has been reported in patients treated for at least 3 months with PPIs and, in most cases, after one year of treatment. Serious adverse events include fatigue, tetany, delirium, dizziness, convulsions, ventricular arrhythmias, and seizures. Treatment of hypomagnesemia in most patients requires magnesium replacement and discontinuation of PPI therapy.

.For patients who are expected to receive long-term therapy or who take PPIs with drugs such as digoxin or with drugs that can cause hypomagnesa (eg diuretics), healthcare professionals may periodically follow magnesium levels before and after starting PPI therapy.

Interactions with studies for neuroendocrine tumors:

Serum chromogranin A (CgA) levels increase as a secondary to drug-induced decreases in gastric acid levels. Elevated CgA levels may lead to false positive results in diagnostic assays for neuroendocrine tumors. Practitioners should temporarily suspend PPI therapy for at least 5 days before assessing CgA levels, and should repeat the test 14 days after discontinuation of PPI therapy if baseline CgA levels are high. If serial tests are being performed (eg for monitoring), the tests should be done in the same laboratory as the reference intervals between tests may vary.

Use with Non-steroidal Anti-inflammatory Drugs (NSAID):

The use of PROTECH to prevent gastroduodenal ulcer induced by non-selective NSAIDs should be limited to patients who need continuous NSAID therapy and are at high risk for developing gastrointestinal complications. High risk should be assessed

according to individual risk factors such as old age (over 65 years old), history of gastric or duodenal ulcer or upper gastrointestinal bleeding episode.

Gastrointestinal infections caused by bacteria

Treatment with proton pump Inhibitors may result in a slightly increased risk of gastrointestinal infections caused by bacteria such as Salmonella and Campylobacter or C. difficile.

Subacute cutaneous lupus erythematosus:

Proton pump inhibitors are very rarely associated with cases of subacute cutaneous lupus erythematosus. Especially in areas exposed to deep sun, when lesions occur and arthralgia is accompanied, the patient should seek immediate medical attention and evaluate the intervention of PROTECH treatment for healthcare professionals. treatment increases the likelihood of being seen with other proton pump inhibitors.

Laboratory tests:

An increased Chromogranin A (CgA) level may affect the investigations for neuroendocrine tumors. To avoid this, PROTECH treatment should be stopped at least 5 days before CgA measurements (See Section 5.1). If CgA and gastrin levels have not returned to the reference range after the first measurement, measurements should be repeated 14 days after discontinuation of proton pump inhibitor therapy.

Alcohol consumption should be avoided during treatment as alcohol may cause irritation of the gastric mucosa.

Sodium: This medicinal product contains 6.7 mg of sodium per tablet. This should be considered for patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

Medicinal products with pH-dependent absorption pharmacokinetics

Due to its severe and prolonged inhibition of gastric acid secretion, PROTECH may affect the absorption of some azole anti-fungals such as ketoconazole, itraconazole, posaconazole and other drugs such as erlotinib, when it is an important determinant in the oral utilization of gastric pH.

HIV protease inhibitors

Concomitant use of pantoprazole with HIV protease inhibitors whose absorption is dependent on acidic intragastric pH, such as atazanavir, is not recommended due to the significant reduction in their bioavailability. (See Section 4.4).

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

Coumarin anticoagulants (phenprocoumon or warfarin)

In clinical pharmacokinetic studies, no interaction was observed during concomitant administration of pantoprazole with phenprocoumon or warfarin. However, very few isolated cases of International Normalized Ratio (INR) changes have been reported among patients receiving PPIs concomitantly with phenprocoumon or warfarin in the post-marketing period. . Increases in INR and prothrombin time can lead to abnormal bleeding and even death. Patients treated with pantoprazole and warfarin or phenprocoumon should be monitored for increases in INR and prothrombin time.

Methotrexate

Concomitant use of high-dose methotrexate (eg 300 mg) and a proton pump inhibitor has been reported to increase methotrexate levels in some patients. Therefore, temporary discontinuation of pantoprazole may need to be considered when using high-dose methotrexate, for example for cancer and psoriasis.

Other interactions studies

PROTECH is extensively metabolized 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 metabolized by the same enzyme system, such as an oral contraceptive containing carbamazepine, diazepam, glibenclamide, nifedipine, levonorgestrel and ethinyl estradiol, do not indicate clinically relevant interactions.

Interaction of pantoprazole with other medicinal products or compounds metabolized using the same enzyme system cannot be excluded.
A number of interaction studies have shown that pantoprazole does not affect the metabolism of active substances metabolized by CYP1A2 (such as caffeine, theophylline), CYP2C9 (such as piroxicam, diclofenac, naproxen), CYP2D6 (such as metoprolol), CYP2E1 (such as ethanol) or the p-glycoprotein-related absorption of digoxin.
No interaction was observed when given with antacids.

In addition, interaction studies have also been conducted on the simultaneous administration of antibiotics such as clarithromycin, metronidazole, amoxicillin with pantoprazole. No clinically significant interactions were observed.

Medicinal products that inhibit or induce CYP2C19:
CYP2C19 inhibitors such as fluvoxamine may increase systemic exposure to pantoprazole. In patients treated with CYP2C19 inhibitors, such as fluvoxamine, or in those with hepatic impairment, a reduction in the dose of pantoprazole may be considered in the long-term use of high doses of pantoprazole.

Enzyme inducers affecting CYP2C19 and CYP3A4, such as rifampicin and St. John's wort (Hypericum perforatum), may decrease the plasma concentrations of PPIs metabolized by these enzyme systems.

Additional information on special populations:

No interaction studies have been conducted on specific populations.

4.6 Pregnancy and lactation

General Recommendation

Pregnancy cathegory: B

Women with childbearing potential / Contraception (Contraception)

No clinically relevant interactions have been observed in specific tests with an oral contraceptive containing levonorgestrel and ethinyl estradiol (see section 4.5).

Pregnancy

Data from a limited number of pregnancy exposure cases (between 300 and 1000 pregnancy outcomes) do not indicate that pantoprozole has adverse effects on pregnancy or on the health of the fetus/newborn child (causing malformations or having foeto/neonatal toxicity). No significant epidemiological data have been obtained to date. Animal studies have shown reproductive toxicity (See Section 5.3).

The potential risk for humans is unknown.

As a precaution, the use of PROTECH during pregnancy should be avoided.

Lactation

Animal studies have shown excretion of pantoprazole in breast milk. Excretion into human milk has been reported. A risk to newborns/infants cannot be excluded. Therefore, the decision whether to continue breastfeeding, or to continue PROTECH treatment, should be made after an assessment of the benefit of breastfeeding to the child and the benefit of PROTECH therapy to the mother.

<u>Reproduction ability / Fertility</u>

There was no evidence of impaired fertility in animal studies following administration of pantoprazole (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). In the event of these adverse events, the patient should not drive or operate machinery.

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 frequency of adverse events listed below, according to system organ class, is defined as follows:

Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).

Adverse reactions in each frequency group are presented in order of decreasing seriousness.

Table 1. Adverse reactions with the use of pantoprazole in clinical studies and post-marketing experience

Frequency / **Organ Systen**	**Common**	**Uncommon**	**Rare**	**Very rare**	**Very rare**
Blood and lymphatic system disorders			Agranulocytosis	Thrombocytopenia; Leukopenia Pancytopenia	
Immune system disorders			Hypersensitivity (including anaphylactic reactions and anaphylactic shock)		
Metabolism and nutrition disorders			Hyperlipidaemias and lipid increases (triglycerides, cholesterol); Weight changes		Hyponatraemia Hipomagnesaemia (See Section 4.4.); Hypocalcemia[(1)]; hypokalemia

Psychiatric disorders		Sleep disorders	Depression (and all aggravations)	Disorientation (and all aggravations)	Hallucination; Confusion (especially in pre-disposed patients, as well as the aggravation of these symptoms in case of pre-existence)
Nervous system disorders		Headache; Dizziness	Taste disorders		Paresthesia
Eye disorders			Disturbances in vision (blurred vision)		
Gastrointestinal disorders	Fundic gland polyps (benign)	Diarrhoea; Nausea /vomiting; Abdominal distension and bloating; Constipation; Dry mouth; Abdominal pain and discomfort			Microscopic colitis
Hepatobiliary disorders		Liver enzymes increased (transaminases, γ-GT)	Bilirubin increased		Hepatocellular injury; Jaundice; Hepatocellular failure
Skin and sub-cutaneous tissue disorders		Rash / exanthema / eruption; Pruritus	Urticaria; Angioedema		Stevens-Johnson syndrome; Lyell syndrome; Erythema multiforme; Photosensitivity; Subacute cutaneous lupus erythematosus (see section 4.4)
Musculoskeletal, connective tissue and bone diseases		Fracture of the hip, wrist or spine (see section 4.4)	Arthralgia; Myalgia		Muscle spasm[(2)]
Kidney and urinary tract diseases					Interstitial nephritis (with possible progression to renal failure)
Reproductive system and breast disorders			Gynecomastia		
General disorders and administration site conditions		Weakness, fatigue and malaise	Body temperature increased; Oedema peripheral		

(1) Hypocalcemia in association with hypomagnesemia

(2) Muscle spasm as a result of electrolyte disturbances

4.9 Overdose

Symptoms of overdose in humans are unknown.
Systemic exposure with up to 240 mg administered intravenously over 2 minutes was well tolerated.

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

In the case of 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: A02BC02
Mechanism of action
Pantoprazol is a substituted benzimidazole which inhibits the secretion of hydrochloric acid in the stomach by specific blockade of the proton pumps of the parietal cells.
Pantoprazol is converted to its active form in the acidic environment in the parietal cells where it inhibits the H+, K+-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 within 2 weeks. As with other proton pump inhibitors and H2 receptor inhibitors, treatment with pantoprazole reduces acidity in the stomach and thereby increases 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, it can inhibit hydrochloric acid secretion independently of stimulation by other substances (acetylcholine, histamine, gastrin). The effect is the same whether the product is given orally or intravenously.

Pharmacodynamic Effects

The fasting gastrin values increase under pantoprazole. On short-term use, in most cases they do not exceed the upper limit of normal. 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, the formation of carcinoid precursors (atypical hyperplasia) or gastric carcinoids as were found in animal experiments (see section 5.3) have not been observed in humans.

During treatment with antisecretory medicinal products, serum gastrin levels are elevated in response to decreased gastric acid release. At the same time, CgA increases due to decreased gastric acidity.

According to some valid published evidence, treatment with proton pump inhibitors should be interrupted 5-14 days before CgA level measurement. B The reason for this application is to allow CgA levels, which have increased due to PPI treatment, to decrease to reference values.

Decreased gastric acidity for any reason, including proton pump inhibitors, results in an increase in the number of bacteria normally present in the gastrointestinal tract.

Treatment with proton pump inhibitors may slightly increase the risk of gastrointestinal infections such as Salmonella and Camphylobacter and possibly also Clostridum difficile in hospitalized patients.

Based on the results of animal studies, the effect of long-term treatment with pantoprazole exceeding one year on the endocrine parameters of the thyroid cannot be completely excluded.

5.2 Pharmacokinetic properties

General features

Absorption:

Pantoprazole is rapidly absorbed and the maximal plasma concentration is achieved even after one single 40 mg oral dose. Serum concentrations of about 2-3 mcg / mL are reached

after a mean of 2.5 hours from administration and these values remain constant after multiple administrations and these values remain constant after multiple applications

Pharmacokinetics does not vary after single or repeated administration.

The absolute bioavailability from the tablet was found to be about 77%. Concomitant intake of food had no influence on AUC, maximum serum concentration and thus bioavailability. Only the variability of the lag-time will be increased by concomitant food intake.

Distribution:

Pantoprazole's serum protein binding is about 98%. Volume of distribution is about 0.15 L/kg.

Biotransformation:

The substance is almost exclusively metabolized in the liver. The main metabolic pathway is demethylation by CYP2C19 with subsequent sulphate conjugation, other metabolic pathway include oxidation by CYP3A4.

Elimination:

The terminal half-life is about one hour and the clearance is about 0.1 l/h/kg. A few cases of delayed elimination have been observed. Due to the specific binding of pantoprazole to the proton pumps of parietal cells, the elimination half-life is not proportional to longer durations of action (inhibition of acid secretion).

Pantoprazole metabolites are excreted mainly by the renal route (approximately 80%), the remainder in the faeces. The main metabolite in both serum and urine is desmethylpantoprazole, which is sulfate-conjugated. The half-life of the main metabolite (approximately 1.5 hours) is no longer than that of pantoprazole.

Linearity / non-linearity:

The pharmacokinetics of PROTECH do not change after single or repeated doses. In the dose range of 10-80 mg, the plasma kinetics of pantoprazole are linear after both oral and intravenous administration.

Characteristics in patients

Poor metabolizers:

About 3% of the European population lack the functional CYP2C19 enzyme and these individuals are termed poor metabolisers. In these individuals, the metabolism of pantoprazole is mainly mediated, probably by the enzyme CYP3A4. After a single dose of 40 mg pantoprazole, the area under the plasma-concentration curve was 6 times greater in poor metabolisers than in subjects with a functional CYP2C19 enzyme (extensive metabolisers). Mean peak plasma concentrations were increased by 60%. These findings are not a recommendation for the posology of pantoprazole.

Kidney failure:

No dose reduction is required for patients with impaired renal function (including dialysis patients). In these patients, as in healthy individuals, pantoprazole has a short half-life and can be dialyzed in very small amounts. Although the half-life of its major metabolite is slightly prolonged (2-3 hours), there is no accumulation since excretion is rapid.

Liver failure:

Although for patients with liver cirrhosis (classes A and B according to Child) the half-life values increased to between 7 and 9 h and the AUC values increased by a factor of 5 - 7, the maximum serum concentration only increased slightly by a factor of 1.5 compared with healthy subjects.

Pediatric Population:

Following administration of single oral doses of 20 or 40 mg pantoprazole to children aged 5 – 16 years AUC and Cmax were in the range of corresponding values in adults.

Following administration of single i.v. 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.

Geriatric Population:

A slight increase in AUC and Cmax in elderly volunteers compared with younger counterparts is also not clinically relevant.

5.3 Preclinical safety data

Preclinical data from conventional pharmacological safety studies, repeated dose toxicity and genotoxicity studies indicate no special hazard for humans.

Neuroendocrine neoplasms were found in carcinogenicity tests performed in rats for 2 years. In addition, scaly cell papillomas were found in the fore stomach of rats.

The mechanism leading to the formation of gastric carcinoids via substituted benzimidazoles has been carefully studied and concluded that increases in serum gastrin levels during chronic high-dose treatment in the rat appear as a secondary reaction. In two-year studies in rodents, an increased number of liver tumors was observed in rats and female mice, which was interpreted to be due to the high hepatic metabolism of pantoprazole.

A slight increase in neoplastic changes of the thyroid was observed in the rat group receiving the highest dose (200 mg/kg). The occurrence of these neoplasms has been associated with pantoprazole-induced changes in the degradation of thyroxine in the rat liver. Since the therapeutic dose in man is low, no harmful effects on the thyroid glands are expected.

In a peri-postnatal rat reproduction study designed to assess bone growth, signs of offspring toxicity (mortality, low mean body weight, low mean body weight gain, and reduced bone development) were observed at exposures (Cmax) of approximately 2 times the human clinical exposure. Bone parameters at the end of the recovery phase were similar between the groups, and body weights also tended to be reversible after the drug-free recovery period. Increased mortality has been reported only in weaned rat pups (up to 21 days) and is estimated to correspond to infants up to 2 years of age. The relevance of this finding to the pediatric population is uncertain. A previous peri-postnatal study in rats at lower doses of 3 mg/kg showed no adverse effects compared to the lower dose of 5 mg/kg.

Studies have not found any evidence of impaired fertility or a teratogenic effect.

Crossing the placenta in the rat has been investigated and found to increase with the progression of pregnancy.

As a result, the fetal pantoprazole concentration increases shortly before birth.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Sodium carbonate, anhydrous
Mannitol
Crospovidone
Povidone K90
Quinoline yellow
Calcium stearate
Hydroxypropyl methyl cellulose
Titanium dioxide
Talc
Polyethylene glycol 400
Sodium lauryl sulfate
Eudragit L-100/55
Triethyl citrate
Colloidal silica anhydrous
Sodium bicarbonate

6.2 Incompatibilities

There is no known incompatibility.

6.3 Shelf Life

36 months.

6.4 Special precautions for storage

It should be stored in a dry place at room temperature below 25°C and protected from light.

6.5 Nature and contents of container

14 or 28 tablet containing PVC/Al/PA – aluminum blisters in carton box

6.6 Instructions for use and handling

No special requirements.

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER AND MANUFACTURER

Marketing Authorisation Holder:

Drogsan İlaçları San. ve Tic. A.Ş.
Oğuzlar Mah. 1370. sok. No: 7/3
06520 Balgat-ANKARA
Tel: 0 312 287 74 10
Fax: 0 312 287 61 15

Manufacturer:

Drogsan İlaçları San. ve Tic. A.Ş.
Esenboğa Merkez Mahallesi, Çubuk Caddesi No:31
06760 Çubuk Ankara / Turkey

8. MARKETING AUTHORISATION NUMBER

026550 (in Georgia)

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

04.10.2013 (in Georgia)

10. DATE OF REVISION OF THE TEXT

09.11.2022