# PROFESSIONAL INFORMATION

**SCHEDULING STATUS** **S4**

## 1. NAME OF THE MEDICINE

**PANTOPRAZOLE UNICORN** 20 (enteric-coated tablets)

**PANTOPRAZOLE UNICORN** 40 (enteric-coated tablets)

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

**PANTOPRAZOLE UNICORN** 20: Each enteric-coated tablet contains pantoprazole sodium sesquihydrate equivalent to 20 mg of pantoprazole.

**PANTOPRAZOLE UNICORN** 40: Each enteric-coated tablet contains pantoprazole sodium sesquihydrate equivalent to 40 mg of pantoprazole.

Sugar free.

For full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Tablets

**PANTOPRAZOLE UNICORN** 20: A yellow, oval, enteric-coated tablet; dimensions approximately 8,9 x 4,6 mm.

**PANTOPRAZOLE UNICORN** 40: A yellow, oval, enteric-coated tablet; dimensions approximately 11,7 x 6,0 mm.

## 4. CLINICAL PARTICULARS

### 4.1 Indications

**PANTOPRAZOLE UNICORN** 40 mg is indicated for the short-term treatment of duodenal ulcer, gastric ulcer and reflux oesophagitis. If the duodenal ulcer has been demonstrated to be associated

with Helicobacter pylori infection, **PANTOPRAZOLE UNICORN** 40 mg used in combination with appropriate antibiotics may be useful.

**PANTOPRAZOLE UNICORN** 40 mg is indicated for the treatment of Zollinger-Ellison Syndrome.

**PANTOPRAZOLE UNICORN** 20 mg is indicated for the symptomatic improvement (e.g. heartburn, acid regurgitation, pain on swallowing) and healing of mild gastro-oesophageal reflux disease (GORD).

**PANTOPRAZOLE UNICORN** 20 mg is indicated for long-term management and prevention of relapse in gastro-oesophageal reflux disease (GORD).

No dosage adjustment is required in the elderly or in the presence of impaired renal and liver function.

**4.2 Posology and method of administration**

**Duodenal ulcer:**

The recommended oral dose is 40 mg of **PANTOPRAZOLE UNICORN** once daily. The total treatment with pantoprazole should be 2 to 4 weeks. If the duodenal ulcer has been demonstrated to be associated with Helicobacter pylori infection, 40 mg of **PANTOPRAZOLE UNICORN** used in combination with appropriate antibiotics may be useful.

**Gastric ulcer:**

The recommended oral dose is 40 mg of **PANTOPRAZOLE UNICORN** once daily for 4 to 8 weeks. In the case of a suspected gastric ulcer, malignancy of the gastric ulcer should be excluded, as treatment could conceal the symptoms and may delay diagnosis.

**Reflux oesophagitis:**

The recommended oral dose is 40 mg of **PANTOPRAZOLE UNICORN** once daily in the morning for 4 to 8 weeks.

**Zollinger-Ellison Syndrome:**

For the management of Zollinger-Ellison Syndrome patients should start their treatment with a daily dose of 80 mg of **PANTOPRAZOLE UNICORN** (two **PANTOPRAZOLE UNICORN** 40 mg tablets). Thereafter, the dosage can be titrated up or down as needed using measurements of gastric acid secretion as a guide. With doses above 80 mg daily, the dose should be divided and given twice daily.

**Mild Gastro-oesophageal reflux disease (GORD):**

The recommended oral dose is 20 mg of **PANTOPRAZOLE UNICORN** per day. A 4-week period is usually required. If this is not sufficient, further 4 weeks of treatment may be used.

**Long-term management and prevention of relapse in GORD:**

For long-term management a maintenance dose of one 20 mg **PANTOPRAZOLE UNICORN** tablet per day is recommended, increasing to 40 mg **PANTOPRAZOLE UNICORN** per day if a relapse occurs. After healing of the relapse, the dose can be reduced to 20 mg of **PANTOPRAZOLE UNICORN**. Experience with long- term administration is limited.

For prevention of gastro-duodenal lesions and dyspeptic symptoms induced by non-selective non-steroidal anti-inflammatory drugs (NSAIDs) in patients at risk and with a need for continuous NSAID treatment, the recommended oral dose is one 20 mg **PANTOPRAZOLE UNICORN** tablet per day.

If symptom control has not been achieved after four weeks of treatment with the prescribed daily dose, further investigation is recommended.

**Special populations:**

**Elderly patients:**

No dosage adjustment is necessary in the elderly.

**Renal and liver function impairment:**

No dosage adjustment is required in the presence of impaired renal function. A daily dose of 20 mg of **PANTOPRAZOLE UNICORN** should not be exceeded in patients with mild to moderately severe liver impairment (see sections 5.2 and 4.4).

**Method of administration**

The recommended once daily dose of **PANTOPRAZOLE UNICORN** should be taken in the morning. **PANTOPRAZOLE UNICORN** should be swallowed whole with a little water either before or during breakfast.

**4.3 Contraindications**

- Hypersensitivity to pantoprazole, substituted benzimidazoles or to any of the other excipients listed in section 6.1.
- Safety and efficacy in children has not been established.
- Co-administration of **PANTOPRAZOLE UNICORN** is not recommended with HIV protease inhibitors for which absorption is dependent on acidic intragastric pH such as atazanavir, nelfinavir; due to significant reduction in their bioavailability (see section 4.5).
- Severely impaired liver function (see section 4.4).

**4.4 Special warnings and precautions for use**

**Influence on vitamin B12 absorption**

In patients with Zollinger-Ellison syndrome and other pathological hypersecretory conditions requiring long-term treatment, **PANTOPRAZOLE UNICORN**, as all acid-blocking medicinal products, 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.

**Co-administration with NSAIDs**

The use of **PANTOPRAZOLE UNICORN** 20 mg as a preventive of gastroduodenal ulcers induced by non-selective non-steroidal anti-inflammatory drugs (NSAIDs) should be restricted to patients who require continued NSAID treatment and have an increased risk to develop gastrointestinal complications. The increased risk should be assessed according to individual risk factors, e.g. high age (>65 years), history of gastric or duodenal ulcer or upper gastrointestinal bleeding.

**Hepatic impairment**

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

**Gastric malignancy**

**PANTOPRAZOLE UNICORN** is not indicated for mild gastrointestinal complaints such as nervous dyspepsia. 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. Diagnosis of reflux oesophagitis should be confirmed by endoscopy.

**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).

**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**

Treatment with pantoprazole may lead to a slightly increased risk of gastrointestinal infections caused by bacteria such as *Salmonella* and *Campylobacter* or *C. difficile*.

**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.

**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 active substances 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.

**Interference with laboratory tests**

Increased Chromogranin A (CgA) level may interfere with investigations for neuroendocrine tumours. To avoid this interference, pantoprazole treatment should be stopped for at least 5 days before CgA measurements (see section 5.1). If CgA and gastrin levels have not returned to reference range after initial measurement, measurements should be repeated 14 days after cessation of proton pump inhibitor treatment.

**4.5 Interaction with other medicines and other forms of interaction**

Concomitant intake of food has no influence on the bioavailability.

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

Because of profound and long lasting inhibition of gastric acid secretion, **PANTOPRAZOLE UNICORN** 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 medicinal products such as erlotinib.

**HIV protease inhibitors**

Co-administration of **PANTOPRAZOLE UNICORN** 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.

**Coumarin anticoagulants (phenprocoumon or warfarin)**

Co-administration of **PANTOPRAZOLE UNICORN** 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 UNICORN** and warfarin or phenprocoumon may need to be monitored for increase in INR and prothrombin time.

**Other interaction studies**

**PANTOPRAZOLE UNICORN** 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 active substances also metabolised with these pathways, like antipyrine, carbamazepine, diazepam, glibenclamide, nifedipine, phenytoin, and an oral contraceptive containing levonorgestrel and ethinyloestradiol did not reveal clinically significant interactions.

An interaction of **PANTOPRAZOLE UNICORN** with other medicines or compounds which are metabolized using the same enzyme system cannot be excluded.

Results from a range of interaction studies demonstrate that **PANTOPRAZOLE UNICORN** 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.

**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.

**4.6 Fertility, pregnancy and lactation**

**Pregnancy**

Safety in pregnancy and during lactation has not been established.

There are no adequate data from the use of **PANTOPRAZOLE UNICORN** in pregnant women.

Studies in animals have shown reproductive toxicity. The potential risk for humans is unknown.

**PANTOPRAZOLE UNICORN** should not be used during pregnancy.

**Breastfeeding**

Animal studies have shown excretion of pantoprazole in breast milk. A risk to the newborns/infants cannot be excluded. Therefore, breastfeeding while on **PANTOPRAZOLE UNICORN** is not recommended.

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

Undesirable effects 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**

**Summary of the safety profile**

Approximately 5 % of patients can be expected to experience undesirable effects. The most commonly reported undesirable effects are diarrhoea and headache, both occurring in approximately 1 % of patients.

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, undesirable effects are presented in order of decreasing seriousness.

**Adverse reactions with pantoprazole in clinical trials and post-marketing experience**

**Blood and lymphatic system:**

***Less frequent*:** Agranulocytosis, leucopoenia, thrombocytopenia, pancytopenia

**Immune system disorders:**

***Less frequent:*** Hypersensitivity (incl. anaphylactic reactions and anaphylactic shock)

**Metabolism and nutrition disorders:**

***Less frequent:*** Hyperlipidaemias and lipid increases (triglycerides, cholesterol), weight changes

***Frequency unknown:*** Hyponatraemia, hypomagnesaemia (see section 4.4), hypocalcaemia[1], hypokalaemia

[1] Hypocalcaemia in association with hypomagnesemia

**Psychiatric disorders:**

***Less frequent*:** Sleep disorders, depression (and all aggravations), disorientation (and all aggravations)

***Frequency unknown:*** Hallucination, confusion (especially in pre-disposed patients, as well as the aggravation of these symptoms in case of pre-existence)

**Nervous system disorders:**

***Less frequent*:** Headache, dizziness, taste disorders

***Frequency unknown:*** Paraesthesia

**Eye disorders**

***Less frequent*:** Disturbances in vision/blurred vision

**Gastrointestinal disorders:**

***Frequent:*** Fundic gland polyps (benign)

***Less frequent*:** Diarrhoea, nausea/vomiting, abdominal distension and bloating, constipation, dry mouth, abdominal pain and discomfort

***Frequency unknown:*** Microscopic colitis

**Hepatobiliary disorders:**

***Less frequent*:** Liver enzymes increased (transaminases, γ-GT), bilirubin increased

***Frequency unknown:*** Hepatocellular injury, jaundice, hepatocellular failure

**Skin and subcutaneous tissue disorders:**

***Less frequent*:** Rash/exanthema/eruption, pruritus, urticaria, angioedema

***Frequency unknown:*** Stevens-Johnson syndrome, Lyell syndrome, erythema multiforme, photosensitivity, drug reaction with eosinophilia and systemic symptoms (DRESS) and subacute cutaneous lupus erythematosus (see section 4.4)

**Musculoskeletal and connective tissue disorders:**

***Less frequent:*** Fracture of the hip, wrist or spine (see section 4.4), arthralgia, myalgia.

***Frequency unknown:*** Muscle spasm as a consequence of electrolyte disturbances

**Renal and urinary disorders:**

***Frequency unknown*:** Interstitial nephritis (with possible progression to renal failure)

**Reproductive system and breast disorders:**

***Less frequent:*** Gynaecomastia

**General disorders and administration site conditions:**

***Less frequent*:** Asthenia, fatigue and malaise, body temperature increased, oedema peripheral

**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. Health care providers are asked to

report any suspected adverse reactions to SAHPRA via the “6.04 Adverse Drug Reactions Reporting Form”, found online under SAHPRA’s publications: https://www.sahpra.org.za/Publications/Index/8 Suspected adverse reactions can also be reported directly to the HCR via Patientsafety.sacg@novartis.com.

**4.9 Overdose**

There are no known symptoms of overdose in man.
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 dialysable.

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**

Pharmacological classification: A 11.4.3 Medicines acting on the gastrointestinal tract

**5.1 Pharmacodynamic properties**

**Mechanism of action**

Pantoprazole 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. Pantoprazole is converted to its active form, a cyclic sulphenamide, 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 receptor level, it can inhibit hydrochloric acid secretion independently of stimulation by other substances (acetylcholine, histamine, gastrin). The effect is the same whether the active substance is given orally or intravenously.

Pantoprazole exerts its full effect in a strongly acidic environment (pH < 3) and remains mostly inactive at higher pH values, which explains its selectivity for the acid secreting parietal cells of the stomach. Therefore, the complete pharmacological and therapeutic effect for pantoprazole can only be achieved in the acid- secreting parietal cells. By means of a feedback mechanism, this effect is diminished at the same rate as acid secretion is inhibited

**Effect on gastric acid secretion:**

Following oral administration, pantoprazole inhibits the pentagastrin stimulated gastric acid secretion. The mean acid inhibition was 85 %, two-and-a-half to three-and-a-half hours after dosing with 40 mg/day for 7 days. Pantoprazole maintains the physiological pH-rhythm. The values, however, are shifted to higher levels. During the night, periods of pH-values approximating placebo have been found to occur.

Although pantoprazole has a half-life of approximately 1 hour, the antisecretory effect increases during repeated once daily administration, demonstrating that the duration of action markedly exceeds the serum elimination half-life.

**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 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.

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

**5.2 Pharmacokinetic properties**

**Absorption:**

Pantoprazole is rapidly absorbed and the maximum plasma concentration is achieved even after one single 20 mg and 40 mg oral dose. On average, at about 2,0 h – 2,5 h p.a. (20 mg pantoprazole) and 2,5 h p.a. (40 mg pantoprazole) the maximum serum concentrations of about 1 to 1,5 µg/ml (20 mg pantoprazole) and 2 to 3 µg/ml (40 mg pantoprazole) are achieved, and these values remain constant after multiple administration.

Pharmacokinetics do not vary after single or repeated administration. In the dose range of 10 to 80 mg the plasma kinetics of pantoprazole are linear after both oral and intravenous 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:**

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

**Elimination:**

Terminal half-life is about 1 hour and clearance is about 0,1 l/h/kg. There were a few cases of subjects with delayed elimination. Because of the specific binding of pantoprazole to the proton pumps of the parietal cell the elimination half-life does not correlate with the much longer duration of action (inhibition of acid secretion).

Renal elimination represents the major route of excretion (approximately 80 %) for the metabolites of pantoprazole, the rest is excreted with the faeces.
The main metabolite in both the serum and urine is desmethylpantoprazole, which is conjugated with sulphate. The half-life of the main metabolite (about 1½ hours), is not much longer than that of pantoprazole.

**Special populations**

***Renal impairment:***

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

***Hepatic impairment:***

Although for patients with liver cirrhosis (classes A and B according to Child), the half-life values increased to between 3 and 6 h (pantoprazole 20 mg) and 7 to 9 hours (pantoprazole 40 mg), and the AUC values increased by a factor of 3-5 (pantoprazole 20 mg) and 5 to 7 (pantoprazole 40 mg), the maximum serum concentration only increased slightly by a factor of 1,3 (pantoprazole 20 mg) and 1,5 (pantoprazole 40 mg) compared with healthy subjects.

***Elderly***

A slight increase in AUC and $C_{max}$ in elderly volunteers compared with younger counterparts is also not clinically relevant.

***Paediatric population***

Following administration of single oral doses of 20 mg 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 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.

**5.3 Preclinical safety data**

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

In the two-year carcinogenicity studies in rats, neuroendocrine neoplasms were found. In addition, squamous cell papillomas were found in the forestomach 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 high-dose 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 pantoprazole's high metabolic rate in the liver.

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

In animal studies (rats) 5 mg/kg was the observed NOAEL (No Observed Adverse Effect Level) for embryotoxicity.

Investigations revealed no evidence of impaired fertility or teratogenic effects.

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

Calcium stearate

Cellulose – microcrystalline

Crospovidone (type A)

Ferric oxide yellow (E172)

Hydroxypropylcellulose (type EXF)

Hypromellose

Macrogol 400

Methacrylic acid - ethyl acrylate copolymer (1:1) dispersion

Opadry yellow

Polysorbate 80

Ponceau 4R aluminium lake (E124)

Quinoline yellow aluminium lake (E104)

Silica – colloidal anhydrous

Sodium carbonate – anhydrous

Sodium lauryl sulfate

Titanium dioxide E171

Triethyl citrate.

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

36 months

### 6.4 Special precautions for storage

Store tightly closed at or below 25 °C.

**KEEP OUT OF THE REACH OF CHILDREN.**

**6.5 Nature and contents of container**

White polyethylene containers with white polypropylene screw cap (tamper evident) with a desiccant insert, containing 14, 28, 30, 56, 100, 250, 300 or 500 tablets.

Aluminium foil and OPA/Al/PVC foil blister strips packed in cardboard cartons, containing 14, 28, 30 or 56 tablets.

Not all pack sizes may be marketed.

**6.6 Special precautions for disposal and other handling**

No special requirements.

**7. HOLDER OF CERTIFICATE OF REGISTRATION**

Sandoz SA (Pty) Ltd[1]

Waterfall 5-Ir

Magwa Crescent West

Waterfall City

Jukskei View

2090

Marketed by **UNICORN PHARMACEUTICALS (PTY) LTD**

**8. REGISTRATION NUMBER(S)**

**PANTOPRAZOLE UNICORN** 20: 43/11.4.3/0485

**PANTOPRAZOLE UNICORN** 40: 43/11.4.3/0486

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

14 September 2012

**10. DATE OF REVISION OF THE TEXT**

13 December 2021

[1]Company Reg. No.: 1990/001979/07