

ANNEX I
SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

PANTOLOC Control 20 mg gastro-resistant tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each gastro-resistant tablet contains 20 mg pantoprazole (as sodium sesquihydrate).

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Gastro-resistant tablet.

Yellow, oval biconvex film-coated tablets imprinted with “P20” in brown ink on one side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

PANTOLOC Control is indicated for short-term treatment of reflux symptoms (e.g. heartburn, acid regurgitation) in adults.

4.2 Posology and method of administration

Posology

The recommended dose is 20 mg pantoprazole (one tablet) per day.

It might be necessary to take the tablets for 2-3 consecutive days to achieve improvement of symptoms. Once complete relief of symptoms has occurred, treatment should be discontinued. The treatment should not exceed 4 weeks without consulting a doctor.

If no symptom relief is obtained within 2 weeks of continuous treatment, the patient should be instructed to consult a doctor.

Special populations

No dose adjustment is necessary in elderly patients or in those with impaired renal or liver function.

Paediatric population

PANTOLOC Control is not recommended for use in children and adolescents below 18 years of age due to insufficient data on safety and efficacy.

Method of administration

PANTOLOC Control 20 mg gastro-resistant tablets should not be chewed or crushed, and should be swallowed whole with liquid before a meal.

4.3 Contraindications

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

Co-administration of Pantoprazole 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).

4.4 Special warnings and precautions for use

Patients should be instructed to consult a doctor if:

- They have unintentional weight loss, anaemia, gastrointestinal bleeding, dysphagia, persistent vomiting or vomiting with blood, since it may alleviate symptoms and delay diagnosis of a severe condition. In these cases, malignancy should be excluded.
- They have had previous gastric ulcer or gastrointestinal surgery.
- They are on continuous symptomatic treatment of indigestion or heartburn for 4 or more weeks.
- They have jaundice, hepatic impairment, or liver disease.
- They have any other serious disease affecting general well-being.
- They are aged over 55 years with new or recently changed symptoms.

Patients with long-term recurrent symptoms of indigestion or heartburn should see their doctor at regular intervals. Especially, patients over 55 years taking any non-prescription indigestion or heartburn remedy on a daily basis should inform their pharmacist or doctor.

Patients should not take another proton pump inhibitor or H₂ antagonist concomitantly.

Patients should consult their doctor before taking this medicinal product if they are due to have an endoscopy or urea breath test.

Patients should be advised that the tablets are not intended to provide immediate relief.

Patients may start to experience symptomatic relief after approximately one day of treatment with pantoprazole, but it might be necessary to take it for 7 days to achieve complete heartburn control. Patients should not take pantoprazole as a preventive medicinal product.

Gastrointestinal infections caused by bacteria

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 medicinal products leads to a slightly increased risk of gastrointestinal infections such as *Salmonella*, *Campylobacter*, or *Clostridium 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 PANTOLOC Control. SCLE after previous treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.

Interference with Laboratory Tests

Increased Chromogranin A (CgA) level may interfere with investigations for neuroendocrine tumours. To avoid this interference, PANTOLOC Control 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.

This medicinal product is intended for short-term use (up to 4 weeks) only (Refer to section 4.2). Patients should be warned about additional risks with long-term use of the medicinal products and the need for prescription and regular surveillance should be emphasized.

The following additional risks are considered relevant for long-term use:

Influence on Vitamin B12 Absorption

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.

Bone Fracture:

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 older people 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.

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.

4.5 Interaction with other medicinal products and other forms of interaction

PANTOLOC Control may reduce the absorption of active substances whose bioavailability is dependent on the gastric pH (e.g. ketoconazole).

HIV Protease Inhibitors:

Co-administration of pantoprazole is contraindicated 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 4.3).

Although no interaction during concomitant administration of phenprocoumon or warfarin has been observed in clinical pharmacokinetic studies, a few isolated cases of changes in International Normalised Ratio (INR) have been reported during concomitant treatment in the post-marketing period. Therefore, in patients treated with coumarin anticoagulants (e.g. phenprocoumon or warfarin), monitoring of prothrombin time/INR is recommended after initiation, termination or during irregular use of pantoprazole.

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.

Pantoprazole is metabolized in the liver via the cytochrome P450 enzyme system. Interaction studies with carbamazepine, caffeine, diazepam, diclofenac, digoxin, ethanol, glibenclamide, metoprolol,

naproxen, nifedipine, phenytoin, piroxicam, theophylline and an oral contraceptive containing levonorgestrel and ethinyl oestradiol did not reveal clinically significant interactions. However, an interaction of pantoprazole with other substances which are metabolised by the same enzyme system cannot be excluded.

There were no interactions with concomitantly administered antacids.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no adequate data from the use of pantoprazole in pregnant women. Studies in animals have shown reproductive toxicity. Preclinical studies revealed no evidence of impaired fertility or teratogenic effects (see section 5.3). The potential risk for humans is unknown. Pantoprazole should not be used during pregnancy.

Breast-feeding

Pantoprazole/metabolites have been identified in human milk. The effect of pantoprazole on newborns/infants is unknown. PANTOLOC Control should not be used during breast-feeding.

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

PANTOLOC Control has no or negligible influence on the ability to drive and use machines. However, adverse reactions such as dizziness and visual disturbances may occur (see section 4.8). If affected, patients should not drive or use machines.

4.8 Undesirable effects

Summary of the safety profile

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

Tabulated list of adverse reactions

The following adverse reactions have been reported with pantoprazole.

Within the following table, adverse reactions are ranked under the MedDRA 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).

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

Frequency System Organ Class	Common	Uncommon	Rare	Very rare	Not known
Blood and lymphatic system disorders			Agranulocytosis	Thrombocytopenia ; Leukopenia, Pancytopenia	
Immune system disorders			Hypersensitivity (incl. anaphylactic reactions and anaphylactic shock)		
Metabolism and nutrition disorders			Hyperlipidaemias and lipid increases (triglycerides, cholesterol); Weight changes		Hyponatraemia, Hypomagnesaemia Hypocalcaemia ⁽¹⁾
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		Paraesthesia
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			

Hepatobiliary disorders		Liver enzymes increased (transaminases, γ -GT)	Bilirubin increased		Hepatocellular injury; Jaundice; Hepatocellular failure
Skin and subcutaneous 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 and connective tissue disorders		Fracture of wrist, hip and spine.	Arthralgia; Myalgia		
Renal and urinary disorders					Interstitial nephritis
Reproductive system and breast disorders			Gynaecomastia		
General disorders and administration site conditions		Asthenia, fatigue and malaise	Body temperature increased; Oedema peripheral		

⁽¹⁾ Hypocalcemia in association with hypomagnesemia

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 the national reporting system listed in [Appendix V](#).

4.9 Overdose

Doses 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 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: Drugs for acid related disorders, Proton pump inhibitors, ATC code: A02BC02

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 heartburn and acid reflux symptoms is achieved in 1 week. 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.

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.

Clinical efficacy

In a retrospective analysis of 17 studies in 5960 patients with gastro-oesophageal reflux disease (GORD) who were treated with 20 mg pantoprazole monotherapy, the symptoms associated with acid reflux e.g. heartburn and acid regurgitation were evaluated according to a standardised methodology. Studies selected had to have at least one acid reflux symptom recording point at 2 weeks. GORD diagnosis in these studies was based on endoscopic assessment, with the exception of one study in which the inclusion of the patients was based on symptomatology alone.

In these studies, the percentage of patients experiencing complete relief from heartburn after 7 days was between 54.0% and 80.6% in the pantoprazole group. After 14 and 28 days, complete heartburn relief was experienced in 62.9% to 88.6% and 68.1% to 92.3% of the patients, respectively.

For the complete relief from acid regurgitation, similar results were obtained as for heartburn. After 7 days the percentage of patients experiencing complete relief from acid regurgitation was between 61.5% and 84.4%, after 14 days between 67.7% and 90.4%, and after 28 days between 75.2% and 94.5%, respectively.

Pantoprazole was consistently shown to be superior to placebo and H2RA and non-inferior to other PPIs. Acid-reflux symptom relief rates were largely independent of the initial GORD stage.

5.2 Pharmacokinetic properties

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.

Absorption

Pantoprazole is completely and rapidly absorbed after oral administration. The absolute bioavailability from the tablet was found to be about 77 %. On average, at about 2.0 h - 2.5 h post administration (t_{max}) of a single 20 mg oral dose, the maximum serum concentrations (C_{max}) of about 1-1.5 $\mu\text{g/ml}$ are achieved, and these values remain constant after multiple administration. Concomitant intake of food had no influence on bioavailability (AUC or C_{max}), but increased the variability of the lag-time (t_{lag}).

Distribution

Volume of distribution is about 0.15 l/kg and serum protein binding is about 98%.

Biotransformation

Pantoprazole is almost exclusively metabolized in the liver.

Elimination

Clearance is about 0.1 l/h/kg, and terminal half-life ($t_{1/2}$) about 1 h. There were a few cases of subjects with delayed elimination. Due to the specific binding of pantoprazole to the proton pumps within 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 (about 80%) for the metabolites of pantoprazole; the rest is excreted with the faeces. The main metabolite in both serum and urine is desmethylpantoprazole, which is conjugated with sulphate. The half-life of the main metabolite (about 1.5 h) 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 patients on dialysis, which removes only negligible amounts of pantoprazole). As with healthy subjects, the half-life of pantoprazole is short. Although the main metabolite has a longer half-life (2-3h), excretion is still rapid and thus accumulation does not occur.

Hepatic impairment

After administration of pantoprazole to patients with liver impairment (Child-Pugh classes A, B and C) the half-life values increased to between 3 and 7 h and the AUC values increased by a factor of 3-6, whereas the C_{max} only increased slightly by a factor of 1.3 compared with healthy subjects.

Elderly

The slight increase in AUC and C_{max} in elderly volunteers compared with younger subjects was not clinically relevant.

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 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 2-year rodent studies an increased number of liver tumors 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 side 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

Core

Sodium carbonate, anhydrous
Mannitol (E421)
Crospovidone
Povidone K90
Calcium stearate

Coating

Hypromellose
Povidone K25
Titanium dioxide (E171)
Yellow iron oxide (E172)
Propylene glycol
Methacrylic acid-ethyl acrylate copolymer (1:1)
Sodium laurilsulfate
Polysorbate 80
Triethyl citrate

Printing ink

Shellac
Red iron oxide (E172)
Black iron oxide (E172)
Yellow iron oxide (E172)
Ammonia solution, concentrated

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

Alu/Alu blisters with or without cardboard reinforcement containing 7 or 14 gastro-resistant tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7. MARKETING AUTHORISATION HOLDER

Takeda GmbH
Byk-Gulden-Str. 2
D-78467 Konstanz
Germany
Telephone: 0800 825332 4
Telefax: 0800 825332 9

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/09/519/001-004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 12 June 2009
Date of latest renewal: 21 February 2014

10. DATE OF REVISION OF THE TEXT

mm/yyyy

Detailed information on this medicinal product is available on the website of the European Medicines Agency <http://www.ema.europa.eu/>.

ANNEX II

- A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

A. MANUFACTURER(S) RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

Takeda GmbH
Production site Oranienburg
Lehnitzstraße 70-98
D-16515 Oranienburg
Germany

Novartis Consumer Health GmbH
Zielstattstraße 40
81379 München
Germany

GSK Consumer Healthcare GmbH & Co. KG,
Barthstrasse 4,
80339 München,
Germany

The printed package leaflet of the medicinal product must state the name and address of the manufacturer responsible for the release of the concerned batch.

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE OF THE MARKETING AUTHORISATION

Medicinal product not subject to medical prescription.

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic Safety Update Reports**

The marketing authorisation holder shall submit periodic safety update reports for this product in accordance with the requirements set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and published on the European medicines web-portal.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk Management Plan (RMP)**

Not applicable.

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON FOR BLISTER

OUTER CARTON FOR BLISTER WITH CARDBOARD REINFORCEMENT

1. NAME OF THE MEDICINAL PRODUCT

PANTOLOC Control 20 mg gastro-resistant tablets
Pantoprazole

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each gastro-resistant tablet contains 20 mg pantoprazole (as sodium sesquihydrate).

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

7 gastro-resistant tablets
14 gastro-resistant tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Tablets should be swallowed whole.
Read the package leaflet before use.
Oral use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Takeda GmbH
Byk-Gulden-Str. 2
D-78467 Konstanz
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/09/519/001-004

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product not subject to medical prescription.

15. INSTRUCTIONS ON USE

For short-term treatment of reflux symptoms (e.g. heartburn, acid regurgitation) in adults.
Take one tablet (20 mg) per day. Do not exceed this dose. This medicine may not bring immediate relief.
Relieves heartburn

16. INFORMATION IN BRAILLE

PANTOLOC Control 20 mg

PARTICULARS TO APPEAR ON THE INTERMEDIATE PACKAGING

CARDBOARD REINFORCEMENT

1. NAME OF THE MEDICINAL PRODUCT

PANTOLOC Control 20 mg gastro-resistant tablets
Pantoprazole

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each gastro-resistant tablet contains 20 mg pantoprazole (as sodium sesquihydrate).

3. LIST OF EXCIPIENTS

4. PHARMACEUTICAL FORM AND CONTENTS

7 gastro-resistant tablets
14 gastro-resistant tablets

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Oral use.
Tablets should be swallowed whole.
Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in the original package in order to protect from moisture.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

Takeda GmbH
Byk-Gulden-Str. 2
D-78467 Konstanz
Germany

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/09/519/001-004

13. BATCH NUMBER

Batch

14. GENERAL CLASSIFICATION FOR SUPPLY

Medicinal product not subject to medical prescription.

15. INSTRUCTIONS ON USE

For short-term treatment of reflux symptoms (e.g. heartburn, acid regurgitation) in adults.
Take one tablet (20 mg) per day. Do not exceed this dose. This medicine may not bring immediate relief.
Relieves heartburn.

16. INFORMATION IN BRAILLE

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

BLISTERS

1. NAME OF THE MEDICINAL PRODUCT

PANTOLOC Control 20 mg gastro-resistant tablets
Pantoprazole

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Takeda GmbH

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. OTHER

B. PACKAGE LEAFLET

Package leaflet: Information for the patient

PANTOLOC Control 20 mg gastro-resistant tablets Pantoprazole

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

Always take this medicine exactly as described in this leaflet or as your doctor or pharmacist have told you.

- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.
- You must talk to a doctor if you do not feel better or if you feel worse after 2 weeks.
- You should not take PANTOLOC Control tablets for more than 4 weeks without consulting a doctor.

What is in this leaflet

1. What PANTOLOC Control is and what it is used for
2. What you need to know before you take PANTOLOC Control
3. How to take PANTOLOC Control
4. Possible side effects
5. How to store PANTOLOC Control
6. Contents of the pack and other information

1. What PANTOLOC Control is and what it is used for

PANTOLOC Control contains the active substance pantoprazole, which blocks the ‘pump’ that produces stomach acid. Hence it reduces the amount of acid in your stomach.

PANTOLOC Control is used for the short-term treatment of reflux symptoms (for example heartburn, acid regurgitation) in adults.

Reflux is the backflow of acid from the stomach into the gullet (“foodpipe”), which may become inflamed and painful. This may cause you symptoms such as a painful burning sensation in the chest rising up to the throat (heartburn) and a sour taste in the mouth (acid regurgitation).

You may experience relief from your acid reflux and heartburn symptoms after just one day of treatment with PANTOLOC Control, but this medicine is not meant to bring immediate relief. It may be necessary to take the tablets for 2-3 consecutive days to relieve the symptoms.

You must talk to a doctor if you do not feel better or if you feel worse after 2 weeks.

2. What you need to know before you take PANTOLOC Control

Do not take PANTOLOC Control:

- if you are allergic to pantoprazole, or to any of the other ingredients of this medicine (listed in section 6).
- if you are taking HIV protease inhibitors such as atazanavir, nelfinavir (for the treatment of HIV-infection). See ‘Other medicines and PANTOLOC Control’.

Warnings and precautions

Talk to your doctor before taking PANTOLOC Control

- if you have been treated for heartburn or indigestion continuously for 4 or more weeks
- if you are over 55 years old and taking non-prescription indigestion treatment on a daily basis
- if you are over 55 years old with any new or recently changed reflux symptoms
- if you have previously had a gastric ulcer or stomach surgery
- if you have liver problems or jaundice (yellowing of skin or eyes)
- if you regularly see your doctor for serious complaints or conditions
- if you are due to have an endoscopy or a breath test called a C-urea test.
- if you have ever had a skin reaction after treatment with a medicine similar to PANTOLOC Control that reduces stomach acid.
- if you are due to have a specific blood test (Chromogranin A)
- If you are taking HIV protease inhibitors such as atazanavir, nelfinavir (for the treatment of HIV-infection) at the same time as pantoprazole, ask your doctor for specific advice.

Do not take this product for longer than 4 weeks without consulting your doctor. If your reflux symptoms (heartburn or acid regurgitation) persist for longer than 2 weeks, consult your doctor who will decide about the need for long-term intake of this medicinal product.

If you take PANTOLOC Control for longer periods, this may cause additional risks, such as:

- reduced absorption of Vitamin B12, and Vitamin B12 deficiency if you already have low body stores of Vitamin B12
- fracture of your hip, wrist or spine, especially if you already suffer from osteoporosis or if you are taking corticosteroids (which can increase the risk of osteoporosis).
- falling magnesium levels in your blood (potential symptoms: fatigue, involuntary muscle contractions, disorientation, convulsions, dizziness, increased heart rate). Low levels of magnesium can also lead to a reduction in potassium or calcium levels in the blood. You should talk to your doctor if you have been using this product for more than 4 weeks. Your doctor may decide to perform regular blood tests to monitor your levels of magnesium.

Tell your doctor immediately, before or after taking this medicine, if you notice any of the following symptoms, which could be a sign of another, more serious, disease:

- an unintentional loss of weight (not related to a diet or an exercise programme)
- vomiting, particularly if repeated
- vomiting blood; this may appear as dark coffee grounds in your vomit
- you notice blood in your stools; which may be black or tarry in appearance
- difficulty in swallowing or pain when swallowing
- you look pale and feel weak (anaemia)
- chest pain
- stomach pain
- severe and/or persistent diarrhoea, because this medicine has been associated with a small increase in infectious diarrhoea.
- If you get a rash on your skin, especially in areas exposed to the sun tell your doctor as soon as you can, as you may need to stop your treatment with PANTOLOC Control. Remember to also mention any other ill-effects like pain in your joints.

Your doctor may decide that you need some tests.

If you are due to have a blood test, tell your doctor that you are taking this medicine.

You may experience relief from your acid reflux and heartburn symptoms after just one day of treatment with PANTOLOC Control, but this medicine is not meant to bring immediate relief. You should not take it as a preventive measure.

If you have been suffering from repetitive heartburn or indigestion symptoms for some time, remember to see your doctor regularly.

Children and adolescents

PANTOLOC Control should not be used by children and adolescents under 18 years of age due to a lack of safety information in this younger age group.

Other medicines and PANTOLOC Control

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines. PANTOLOC Control may stop certain other medicines from working properly. Especially medicines containing one of the following active substances:

- HIV protease inhibitors such as atazanavir, nelfinavir (for the treatment of HIV-infection). You must not use PANTOLOC Control if you are taking HIV protease inhibitors. See 'Do not take PANTOLOC Control'.
- ketoconazole (used for fungal infections).
- warfarin and phenprocoumon (used to thin blood and prevent clots). You may need further blood tests
- methotrexate (used to treat rheumatoid arthritis, psoriasis, and cancer) – if you are taking methotrexate your doctor may temporarily stop your PANTOLOC Control treatment because pantoprazole can increase levels of methotrexate in the blood.

Do not take PANTOLOC Control with other medicines which limit the amount of acid produced in your stomach, such as another proton pump inhibitor (omeprazole, lansoprazole or rabeprazole) or an H2 antagonist (e.g. ranitidine, famotidine).

However, you may take PANTOLOC Control with antacids (e.g. magaldrate, alginic acid, sodium bicarbonate, aluminium hydroxide, magnesium carbonate, or combinations thereof), if needed.

Pregnancy and breast-feeding

You should not take this medicine if you are pregnant or while-breastfeeding.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines

If you experience side effects like dizziness or disturbed vision, you should not drive or use machines.

3. How to take PANTOLOC Control

Always take this medicine exactly as described in this leaflet or as your doctor or pharmacist have told you. Check with your doctor or pharmacist if you are not sure.

The recommended dose is one tablet a day. Do not exceed this recommended dose of 20 mg pantoprazole daily.

You should take this medicine for at least 2-3 consecutive days. Stop taking PANTOLOC Control when you are completely symptom-free. You may experience relief from your acid reflux and heartburn symptoms after just one day of treatment with PANTOLOC Control, but this medicine is not meant to bring immediate relief.

If you have no symptom-relief after taking this medicine for 2 weeks continuously, consult your doctor.

Do not take PANTOLOC Control tablets for more than 4 weeks without consulting your doctor.

Take the tablet before a meal, at the same time every day. You should swallow the tablet whole with some water. Do not chew or break the tablet.

If you take more PANTOLOC Control than you should

Tell your doctor or pharmacist if you have taken more than the recommended dose. If possible take your medicine and this leaflet with you.

If you forget to take PANTOLOC Control

Do not take a double dose to make up for the forgotten dose. Take your next, normal dose, the next day, at your usual time.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your doctor immediately or contact the casualty department at your nearest hospital, if you get any of the following **serious side effects**. Stop taking this medicine straight away, but take this leaflet and/or the tablets with you.

- **Serious allergic reactions (rare: may affect up to 1 in 1,000 people):** Hypersensitivity reactions, so-called anaphylactic reactions, anaphylactic shock and angioedema. Typical symptoms are: swelling of the face, lips, mouth, tongue and/or throat, which may cause difficulty in swallowing or breathing, hives (nettle rash), severe dizziness with very fast heartbeat and heavy sweating.
- **Serious skin reactions (frequency not known: frequency cannot be estimated from the available data):** rash with swelling, blistering or peeling of the skin, losing skin and bleeding around eyes, nose, mouth or genitals and rapid deterioration of your general health, or rash when exposed to the sun.
- **Other serious reactions (frequency not known):** yellowing of the skin and eyes (due to severe liver damage), or kidney problems such as painful urination and lower back pain with fever.

Other side effects include:

- **Common** (may affect up to 1 in 10 people): Benign polyps in the stomach
- **Uncommon side effects (may affect up to 1 in 100 people):** headache; dizziness; diarrhoea; feeling sick, vomiting; bloating and flatulence (wind); constipation; dry mouth; bellyache and discomfort; skin rash or hives; itching; feeling weak, exhausted or generally unwell; sleep disorders; increase in liver enzymes in a blood test; fracture in the hip, wrist or spine.
- **Rare side effects:** distortion or complete lack of the sense of taste; disturbances in vision such as blurred vision; pain in the joints; muscle pains; weight changes; raised body temperature; swelling of the extremities; depression; increased bilirubin and fat levels in blood (seen in blood tests), breast enlargement in males; high fever and a sharp drop in circulating granular white blood cells (seen in blood tests).
- **Very rare side effects (may affect up to 1 in 10,000 people):** disorientation; reduction in the number of blood platelets, which may cause you to bleed or bruise more than normal; reduction in the number of white blood cells, which may lead to more frequent infections; coexisting abnormal reduction in the number of red and white blood cells, as well as platelets (seen in blood tests).

- **Frequency not known:**
hallucination, confusion (especially in patients with a history of these symptoms); decreased level of sodium in blood; decreased level of magnesium in blood, rash, possibly with pain in the joints; feeling of tingling, prickling, pins and needles, burning sensation or numbness.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via [the national reporting system](#) listed in [Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store PANTOLOC Control

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date, which is stated on the carton and the blister after 'EXP'. The expiry date refers to the last day of that month.

Store in the original package in order to protect from moisture.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What PANTOLOC Control contains

- The active substance is pantoprazole. Each tablet contains 20 mg pantoprazole (as sodium sesquihydrate).
- The other ingredients are:
 - Core: sodium carbonate (anhydrous), mannitol, crospovidone, povidone K90, calcium stearate.
 - Coating: hypromellose, povidone, titanium dioxide (E171), yellow iron oxide (E172), propylene glycol, methacrylic acid-ethyl acrylate copolymer, sodium lauril sulfate, polysorbate 80, triethyl citrate.
 - Printing ink: shellac, red, black and yellow iron oxide (E172), and ammonia solution, concentrated.

What PANTOLOC Control looks like and contents of the pack

The gastro-resistant tablets are yellow, oval, biconvex film-coated tablets imprinted with "P20" on one side.

PANTOLOC Control is available in Alu/Alu blisters with or without cardboard reinforcement.

Packs containing 7 or 14 gastro-resistant tablets. Not all pack sizes may be marketed.

Marketing Authorisation Holder

Takeda GmbH
Byk-Gulden-Straße 2, 78467 Konstanz
Germany

Manufacturer

Takeda GmbH
Production site Oranienburg
Lehnitzstraße 70-98, 16515 Oranienburg
Germany

Novartis Consumer Health GmbH
Zielstattstraße 40
81379 München
Germany

GSK Consumer Healthcare GmbH & Co. KG,
Barthstrasse 4,
80339 München,
Germany

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien

Takeda Belgium
Tél/Tel: + 32 2 464 06 11
takeda-belgium@takeda.com

Lietuva

Takeda, UAB
Tel: +370 521 09070
lt-info@takeda.com

България

Такеда България
Тел.: + 359 (2) 958 27 36

Luxembourg/Luxemburg

Takeda Belgium
Tél/Tel: + 32 2 464 06 11
takeda-belgium@takeda.com

Česká republika

GlaxoSmithKline Consumer Healthcare s.r.o.
Tel: + 420 222 001 111

Magyarország

GlaxoSmithKline-Consumer Kft.
Tel.: 06-1-22-55-800
Fax : 06-1-22-55-802

Danmark

GlaxoSmithKline Consumer Healthcare A/S
Tlf: + 45 44 86 86 86

Malta

Takeda Italia S.p.A.
Tel: +39 06 502601

Deutschland

Takeda GmbH
Tel: 0800 825 3324
medinfo@takeda.de

Nederland

Takeda Nederland bv
Tel: +31 23 56 68 777
nl.medical.info@takeda.com

Eesti

Takeda Pharma AS
Tel: +372 617 7669
info@takeda.ee

Norge

GlaxoSmithKline Consumer Healthcare A/S
Tlf : +47 22 70 20 00

Ελλάδα

TAKEDA ΕΛΛΑΣ Α.Ε
Τηλ: +30 210 6729570
gr.info@takeda.com

Österreich

Takeda Pharma Ges.m.b.H.
Tel: +43 (0)800-20 80 50

España

GlaxoSmithKline Consumer Healthcare, S.A.
Tel: + 34 900 101 309

Polska

Takeda Polska Sp. z o.o.
Tel.: + 48 22 608 13 00

France

GLAXOSMITHKLINE SANTE GRAND
PUBLIC S.A.S.
Tél: + 33 1 39 17 80 00

Portugal

GlaxoSmithKline Consumer Healthcare, Produtos
para a Saúde e Higiene, Lda.
Tel: + 351 800 784 695

Hrvatska

Takeda Pharmaceuticals
Croatia d.o.o.
Tel: +385 1 377 88 96

Ireland

GlaxoSmithKline Consumer Healthcare (UK)
United Kingdom
Tel: +353 1 495 5000
Medical Information Direct Line: 1800 441 442

Ísland

GlaxoSmithKline Consumer Healthcare A/S
Danmörk
Sími: + 45 44 86 86 86

Italia

GlaxoSmithKline Consumer Healthcare S.p.A
Tel: + 39 02 38061

Κύπρος

TAKEDA ΕΛΛΑΣ Α.Ε
Τηλ: +30 210 6729570
gr.info@takeda.com

Latvija

Takeda Latvia SIA
Tel: + 371 67840082

România

Takeda Pharmaceuticals SRL
Tel: + 40 21 335 03 91

Slovenija

Takeda GmbH, Podružnica Slovenija
Tel: + 386 (0) 59082480

Slovenská republika

GlaxoSmithKline Consumer Healthcare s.r.o.
Česká republika
Tel: + 420 222 001 111

Suomi/Finland

GlaxoSmithKline Consumer Healthcare Finland
Oy
Puh/Tel: + 35 8 10 303 030

Sverige

GlaxoSmithKline Consumer Healthcare A/S
Tel: +46 20-10 05 79

United Kingdom

GlaxoSmithKline Consumer Healthcare (UK)
Medical Information Direct Line: 0800 783 8881

This leaflet was last revised in { mm/yyyy }

Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu/>.

The following recommendations for lifestyle and dietary changes may also help to relieve heartburn or acid related symptoms.

- Avoid large meals
- Eat slowly
- Stop smoking
- Reduce alcohol and caffeine consumption
- Reduce weight (if overweight)
- Avoid tight-fitting clothing or belts
- Avoid eating less than three hours before bedtime
- Elevate bedhead (if you suffer from nocturnal symptoms)
- Reduce intake of food that can cause heartburn. These might include: Chocolate, peppermint, spearmint, fatty and fried food, acidic food, spicy food, citrus fruits and fruit juices, tomatoes.

ANNEX IV

**SCIENTIFIC CONCLUSIONS AND GROUNDS FOR THE VARIATION TO THE TERMS
OF THE MARKETING AUTHORISATION(S)**

Scientific conclusions

Taking into account the PRAC Assessment Report on the PSUR(s) for pantoprazole, the scientific conclusions of CHMP are as follows:

A cumulative search of the safety database for potential cases of paraesthesia using updated search criteria up to 31 January 2018 was performed. This yielded 711 case reports with 852 events. From the 711 cases, 131 cases were serious. 485 out of 711 cases were considered related to treatment with pantoprazole.

Positive de-challenge was recorded in 190 cases, 172 of which were considered related to pantoprazole (as determined by the company). The events in 28 of these 172 cases were serious. There were 44 cases of negative de-challenge overall, 25 of which were considered to be related to treatment with pantoprazole. Of these related cases, 8 were serious and 17 were classified as non-serious.

Due to the number of cases with a positive dechallenge paraesthesia, the product information of pantoprazole containing medicinal product should ensure that paraesthesia is added as an adverse drug reaction with unknown frequency in section 4.8 of the SmPC. The package leaflet should be updated accordingly, if applicable.

Cumulatively there have been 55 serious cases of hypocalcaemia of which a significant number were associated with the known side effect of hypomagnesaemia. Based on this information, "hypocalcaemia in association with hypomagnesaemia" should be included in section 4.8 of the SmPC of all pantoprazole-containing medicinal products. The package leaflet should be updated accordingly, if applicable.

The CHMP agrees with the scientific conclusions made by the PRAC.

Grounds for the variation to the terms of the marketing authorisation(s)

On the basis of the scientific conclusions for pantoprazole the CHMP is of the opinion that the benefit-risk balance of the medicinal product(s) containing pantoprazole is unchanged subject to the proposed changes to the product information

The CHMP recommends that the terms of the marketing authorisation(s) should be varied.