ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

SOMAC Control 20 mg gastro-resistant tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

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

Excipient: contains 1.06 microgram soya lecithin per gastro-resistant tablet.
For a 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

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 use
SOMAC 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
SOMAC 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, to soya or to any of the other excipients (see section 6.1).

Co-administration with atazanavir (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 H_2 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.

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 C. difficile.

4.5 Interaction with other medicinal products and other forms of interaction

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

It has been shown that co-administration of atazanavir 300 mg/ritonavir 100 mg with omeprazole (40 mg once daily) or atazanavir 400 mg with lansoprazole (60 mg single dose) to healthy volunteers resulted in a substantial reduction in the bioavailability of atazanavir. The absorption of atazanavir is pH-dependent. Therefore, pantoprazole must not be co-administered with atazanavir (see section 4.3).

Pantoprazole is metabolized in the liver via the cytochrome P450 enzyme system. An interaction of pantoprazole with other substances which are metabolized by the same enzyme system cannot be excluded. However, no clinically significant interactions were observed in specific tests with carbamazepine, caffeine, diazepam, diclofenac, digoxin, ethanol, glibenclamide, metoprolol, naproxen, nifedipine, phenytoin, piroxicam, theophylline and an oral contraceptive containing levonorgestrel and ethinyl oestradiol.

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.

There were no interactions with concomitantly administered antacids.

4.6 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. This medicinal product should not be used during pregnancy.

Lactation
It is unknown whether pantoprazole is excreted in human breast milk. Animal studies have shown excretion of pantoprazole in breast milk. This medicinal product should not be used during breast-feeding.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Approximately 5% of patients can be expected to experience adverse drug reactions (ADRs). The most commonly reported ADRs are diarrhoea and headache, both occuring in approximately 1% of patients. The following undesirable effects have been reported with pantoprazole.

Within the following table, undesirable effects are ranked under the following frequency classification:

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).

Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness.

Table 1. Undesirable effects with pantoprazole in clinical trials and post-marketing experience

Frequency / **System Organ Class**	**Uncommon**	**Rare**	**Very rare**	**Not known**
Blood and lymphatic system disorders			Thrombocytopenia; Leukopenia	
Nervous system disorders	Headache; Dizziness			
Eye disorders		Disturbances in vision / blurred vision		
Gastrointestinal disorders	Diarrhoea; Nausea / vomiting; Abdominal distension and bloating; Constipation; Dry mouth; Abdominal pain and discomfort			
Renal and urinary disorders				Interstitial nephritis
Skin and subcutaneous tissue disorders	Rash / exanthema / eruption; Pruritus	Urticaria; Angioedema		Stevens-Johnson syndrome; Lyell syndrome; Erythema multiforme; Photosensitivity
Musculoskeletal and connective tissue disorders		Arthralgia; Myalgia		
Metabolism and nutrition disorders		Hyperlipidaemias and lipid increases (triglycerides, cholesterol); Weight changes		Hyponatraemia
General disorders and administration site conditions	Asthenia, fatigue and malaise	Body temperature increased; Oedema peripheral		
Immune system disorders		Hypersensitivity (incl. anaphylactic reactions and anaphylactic shock)		
Hepatobiliary disorders	Liver enzymes increased (transaminases, γ-GT)	Bilirubin increased		Hepatocellular injury; Jaundice; Hepatocellular failure

Frequency / System Organ Class	Uncommon	Rare	Very rare	Not known
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)

4.9 Overdose

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

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 µg/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%.

Metabolism and excretion
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).

Pantoprazole is almost exclusively metabolized in the liver. 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

Preclinical data reveal no special hazard to 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)
Soya lecithin
Titanium dioxide (E171)

Antifoam DC 1510

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 containing 7 or 14 gastro-resistant tablets or Alu/Alu blisters with cardboard reinforcement containing 7 or 14 gastro-resistant tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Nycomed GmbH
Byk-Gulden-Str. 2
D-78467 Konstanz
Germany
Telephone: +49-(0)7531-84-0
Telefax: +49-(0)7531-84-2474

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency (EMEA) http://www.emea.europa.eu/.

ANNEX II

A. MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE

B. CONDITIONS OF THE MARKETING AUTHORISATION

A. MANUFACTURING AUTHORISATION HOLDER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer responsible for batch release

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

B. CONDITIONS OF THE MARKETING AUTHORISATION

- **CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE IMPOSED ON THE MARKETING AUTHORISATION HOLDER**

Medicinal product not subject to medical prescription.

- **CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

Not applicable.

- **OTHER CONDITIONS**

Pharmacovigilance system

The MAH must ensure that the system of pharmacovigilance, as described in version 3.0 dated 07.11.2008 presented in Module 1.8.1. of the Marketing Authorisation Application, is in place and functioning before and whilst the product is on the market.

PSUR

The PSUR submission schedule for SOMAC Control 20 mg gastro-resistant tablets should follow the PSUR submission schedule of the reference medicinal product.

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

SOMAC 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

Contains soya lecithin. See leaflet for further information.

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 REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight 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

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

12. MARKETING AUTHORISATION NUMBER(S)

EU/0/00/000/000

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

SOMAC Control 20 mg

PARTICULARS TO APPEAR ON THE INTERMEDIATE PACKAGING

CARDBOARD REINFORCEMENT

1. NAME OF THE MEDICINAL PRODUCT

SOMAC 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

Contains soya lecithin. See leaflet for further information.

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 REACH AND SIGHT OF CHILDREN

Keep out of the reach and sight 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

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

12. MARKETING AUTHORISATION NUMBER(S)

EU/0/00/000/000

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

SOMAC Control 20 mg gastro-resistant tablets
Pantoprazole

2. NAME OF THE MARKETING AUTHORISATION HOLDER

Nycomed GmbH

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Batch

5. OTHER

B. PACKAGE LEAFLET

PACKAGE LEAFLET: INFORMATION FOR THE USER

SOMAC Control 20 mg gastro-resistant tablets
Pantoprazole

Read all of this leaflet carefully because it contains important information for you.
This medicine is available without prescription. However, you still need to use SOMAC Control carefully to get the best results from it.
- Keep this leaflet. You may need to read it again.
- Ask your pharmacist if you need more information or advice.
- You must contact a doctor if your symptoms worsen or do not improve after 2 weeks.
- You should not take SOMAC Control tablets for more than 4 weeks without consulting a doctor.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT SOMAC CONTROL IS AND WHAT IT IS USED FOR

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

SOMAC 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 SOMAC 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.

2. BEFORE YOU TAKE SOMAC CONTROL

Do not take SOMAC Control:
- if you are allergic (hypersensitive) to pantoprazole, to soya or to any of the other ingredients of SOMAC Control (listed in section 6 'What SOMAC Control contains').
- if you are taking a medicine containing atazanavir (for the treatment of HIV-infection)
- if you are under 18 years of age
- if you are pregnant or breast-feeding.

Take special care with SOMAC Control
Talk to your doctor first if:
- you have been treated for heartburn or indigestion continuously for 4 or more weeks
- you are over 55 years old and taking non-prescription indigestion treatment on a daily basis
- you are over 55 years old with new or recently changed symptoms
- you have previously had a gastric ulcer or stomach surgery

- you have liver problems or jaundice (yellowing of skin or eyes)
- you regularly see your doctor for serious complaints or conditions
- you are due to have an endoscopy or a breath test called a C-urea test.

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 SOMAC Control has been associated with a small increase in infectious diarrhoea.

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 SOMAC 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.

Using other medicines
SOMAC Control may stop certain other medicines from working properly. Tell your doctor or pharmacist if you are using any medicines containing one of the following active substances:
- ketoconazole (used for fungal infections).
- warfarin and phenprocoumon (used to thin blood and prevent clots). You may need further blood tests
- atazanavir (used to treat HIV-infection). You must not use SOMAC Control if you are taking atazanavir.

Do not take SOMAC 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 SOMAC Control with antacids (e.g. magaldrate, alginic acid, sodium bicarbonate, aluminium hydroxide, magnesium carbonate, or combinations thereof), if needed.

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. This also includes herbal or homeopathic remedies.

Using SOMAC Control with food and drink
The tablets should be swallowed whole with liquid before a meal.

Pregnancy and breast-feeding
Do not take SOMAC Control if you are pregnant, think you may be pregnant, or are breast-feeding. Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines
If you experience side effects like dizziness or disturbed vision, you should not drive or operate machines.

Important information about some of the ingredients of SOMAC Control
SOMAC Control contains soya lecithin. If you are allergic to peanut or soya, do not use this medicine.

3. HOW TO TAKE SOMAC CONTROL

Always take SOMAC Control exactly as described in this leaflet. You should check with your doctor or pharmacist if you are not sure.

Take 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 SOMAC 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 SOMAC 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 SOMAC 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.

Children and adolescents
SOMAC Control should not be used by children and young people under 18 years of age.

If you take more SOMAC Control than you should
Tell your doctor or pharmacist straight away. If possible take your medicine and this leaflet with you. There are no known symptoms of overdose.

If you forget to take SOMAC 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 product, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, SOMAC Control 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)**: 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)**: 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.

Side effects may occur with certain frequencies, which are defined as follows:
- very common: affects more than 1 user in 10
- common: affects 1 to 10 users in 100

- uncommon: affects 1 to 10 users in 1,000
- rare: affects 1 to 10 users in 10,000
- very rare: affects less than 1 user in 10,000
- not known: frequency cannot be estimated from the available data.

- **Uncommon side effects**:
  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.

- **Rare side effects**:
  disturbances in vision such as blurred vision; pain in the joints; muscle pains; weight changes; raised body temperature; swelling of the extremities; allergic reactions; depression; increased bilirubin and fat levels in blood (seen in blood tests).

- **Very rare side effects**:
  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.

- **Frequency not known**:
  hallucination, confusion (especially in patients with a history of these symptoms); decreased level of sodium in blood.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE SOMAC CONTROL

Keep out of the reach and sight of children.

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

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

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What SOMAC 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), soya lecithin, titanium dioxide (E 171) and antifoam DC 1510.

What SOMAC 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.
SOMAC 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
Nycomed GmbH
Byk-Gulden-Straße 2, 78467 Konstanz
Germany

Manufacturer
Nycomed GmbH
Production site Oranienburg
Lehnitzstraße 70-98, 16515 Oranienburg
Germany

For any information about this medicine, please contact the Marketing Authorisation Holder.

This leaflet was last approved in

Detailed information on this medicine is available on the European Medicines Agency (EMEA) web site: http://www.emea.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 REFUSAL ON THE CLAIM FOR ONE-YEAR DATA EXCLUSIVITY PRESENTED BY THE EMEA

SCIENTIFIC CONCLUSIONS AND GROUNDS FOR REFUSAL ON THE CLAIM FOR ONE-YEAR DATA EXCLUSIVITY PRESENTED BY THE EMEA

With reference to Article 74a of Directive 2001/83/EC, as amended, the applicant requested one year data exclusivity for the data submitted for the change of the classification of the medicinal product from prescription to non-prescription. Such exclusivity requires that the change of classification "has been authorised on the basis of significant preclinical tests or clinical trials".

The justification of the applicant was based on 6 'non-published' studies, 5 full and one published by abstract only, which have been provided in support of the application (BY1023/BGI022, BY1023/BF010, BY1023/ESP009, BY1023/MEX020, BY1023/FK3037 and BY1023/VMG309). It was stated that these 6 studies support the proposed new indication and treatment duration by providing at least one symptom recording point of reflux-related symptoms during the first 14 days of treatment with pantoprazole and therefore are considered significant for the application. Study BY1023/BGI022 was particularly emphasised. During the procedure, the applicant further substantiated the justification. The applicant emphasised that these studies demonstrated efficacy in the non-prescription setting regarding the proposed indication and related posology which differs from that of the prescription product. The applicant, in addition to study BGI022 (CSR 257/2004), referred to study MEX020 (CSR 200/2004). The applicant also referred to studies BF010 (CSR 298E/99) and VMG309 (CSR 323/2004) which were considered to provide data for early onset of relief of reflux symptoms. Overall the applicant considered that the new data from the aforementioned studies added significant support to the classification as non-prescription product as they provided both effect and relevance to the assessment.

The CHMP reviewed the clinical data submitted, taking into account the provisions of Article 74a of Directive 2001/83/EC, as amended, in support of the classification of SOMAC Control 20 mg gastro-resistant tablets as 'medicinal product not subject to medical prescription'.

Out of the 17 studies submitted in support of the application, the following 11 studies did not form the basis of the applicant's request for data exclusivity:

Study No. ***(CSR No.)***	**Primary Objective**	**Secondary Objective**	**Treatment**	**Duration**	**N (ITT)**	**Results**
BY1023/BGSA017 ***(245/98)***	Relief of heartburn in GORD Stage 0	Time to freedom from key GORD symptoms	Pan 20, Placebo	2 weeks	219	Pantoprazole was superior to placebo
BY1023/FK3059 ***(93/2001)***	Relief of key symptoms in GORD after 28 days	Relief of key symptoms in GORD after 14 days	Pan 20, Ran 300 once daily	4 weeks	338	Pantoprazole was superior to ranitidine
BY1023/VMG306 ***(302/98)***	Relief of symptoms in GORD Stage 0/I after 4 weeks of treatment	Leading symptom relief after 2 weeks of treatment	Pan 20, Ran 150 bid	4 weeks	356	Pantoprazole was superior to ranitidine
BY1023/VMG305 ***(301/98)***	Relief of symptoms in GORD Stage 0/I after 4 weeks of treatment	Relief of GORD symptoms after 2 weeks of treatment	Pan 20, Lan 15	4 weeks	375	Pantoprazole was non-inferior to lansoprazole after 4 weeks of treatment
BY1023/M3-316 ***(152/2003)***	Relief of symptoms in GORD Stage A-D	Assessment of GI symptoms at day 14 and 28	Pan 20, 40	4 weeks	421	Pantoprazole was effective and well tolerated
BY1023/M3-320 ***(170/2003)***	Time to first symptom relief of GORD-related symptoms in GORD Stage 0	Relief of GORD-related symptoms after 14 and 28 days	Pan 20, Eso 20	4 weeks	529	Both PPIs were comparably effective; pantoprazole was non-inferior to esomeprazole

BY1023/FK3034 ***(166/95)***	Endoscopic healing of GORD Stage I	Relief of leading GORD symptoms and other GI symptoms	Pan 20, Ran 300 once daily	4/8 weeks	209	Pantoprazole was significantly more effective than ranitidine
BY1023/BGSA006 ***(208/95)***	Endoscopic healing of GORD Stage I	Relief of leading GORD symptoms and other GI symptoms	Pan 20, Ran 300 once daily	4/8 weeks	201	Pantoprazole was significantly more effective than ranitidine
3001A1-300-US ***(319E/98)***	Endoscopic healing erosive esophagitis	Relief of typical GORD symptoms	Pan 10, 20, 40, Pla	4/8 weeks	603	Pantoprazole was significantly more effective than placebo
3001A1-301-US ***(320E/98)***	Endoscopic healing erosive esophagitis	Relief of typical GORD symptoms	Pan 20, 40, Niz 150 bid	4/8 weeks	243	Pantoprazole was significantly more effective than nizatidine
BY1023/UK005 ***(303/98)***	Endoscopic healing of GORD Stage I after 4 weeks	Endoscopic healing of GORD Stage I after 8 weeks, Improvement of GORD symptoms after 2 and 4 weeks	Pan 20, Ome 20	4/8 weeks	327	Pantoprazole and omeprazole were similarly effective

CSR = Clinical Study Report, N = Number of Patients, Eso = Esomeprazole, Lan = Lansoprazole,
Niz = Nizatidine, Ome = Omeprazole, Pan = Pantoprazole, Pla = Placebo, Ran = Ranitidine, bid =twice daily

Based on the above results the CHMP considered the following:

- pantoprazole 20mg is effective in the short-term treatment of GORD symptoms
- the applicant's justification to extrapolate the results of these studies to the proposed non-prescription setting is acceptable
- the safety profile of pantoprazole is well established and acceptable.

Out of the 17 studies provided by the applicant, the following 6 studies formed the basis of the applicant's request for data exclusivity:

Study No. ***(CSR No.)***	**Primary Objective**	**Secondary Objective**	**Treatment**	**Duration**	**N (ITT)**	**Results**	**Comments**
BY1023/BGI022 ***(257/2004)***	Relief of heartburn in GORD Stage 0/I at day 14	Relief of heartburn in GORD Stage 0/I at day 28	Pan 20, Ran 150 bid	4 weeks	344	Pantoprazole was superior to ranitidine in the relief of GORD symptoms	Results are similar to published studies (FK3059, VMG306, FK3034 and BGSA006)
BY1023/BF010 ***(298E/99)***	Relief of heartburn in GORD Stage 0	Quality of life, Time to heartburn relief	Pan 20, Ome 10	4/8 weeks	331	Both medications were similarly effective	Published studies showed non-inferiority of pantoprazole compared to other PPIs (Study VMG305 and M3-320)
BY1023/VMG309 ***(323/2004)***	Relief of heartburn in GORD Stage I after 1 and 2 weeks of treatment	Relief of GORD symptoms, Time to heartburn relief	Pan 20, Ome 10	2 weeks	521	Both PPIs were comparably effective; pantoprazole was non-inferior to omeprazole, non-significant primary endpoint	Published studies suggest non-inferiority of pantoprazole compared to other PPIs (Study VMG305 and M3-320)

BY1023/ESP009 ***(396/2004)***	Endoscopic healing of GORD Stage I after 8 weeks of treatment	Endoscopic healing of GORD Stage I after 4 weeks of treatment	Pan 20, Ran 150 bid	4/8 weeks	270	Pantoprazole was superior to ranitidine	Results are similar to published studies (FK3059, VMG306, FK3034 and BGSA006)
BY1023/MEX020 ***(200/2004)***	Endoscopic healing of GORD Stage I	Relief of GORD symptoms after 7 and 28 days of treatment	Pan 20, Ome 10	4/8 weeks	346	Pantoprazole and omeprazole were similarly effective	Published studies showed non-inferiority of pantoprazole compared to other PPIs (Study VMG305 and M3-320)
BY1023/FK3037 ***(105/96)***	Endoscopic healing of GORD Stage II/III after 4 and 8 weeks of treatment	Symptom relief at 2 and 4 weeks of treatment	Pan 20, 40, 80	4/8 weeks	322	There was no statistically significant difference between the treatment groups	Similar results were shown in the published study M3-316.

CSR = Clinical Study Report, N = Number of Patients, Eso = Esomeprazole, Lan = Lansoprazole, Niz = Nizatidine, Ome = Omeprazole, Pan = Pantoprazole, Pla = Placebo, Ran = Ranitidine, bid =twice daily

With reference to the above 6 studies, the CHMP made the following observations (see also comments included in the above table):

- BGI022 (CSR 257/2004)
  In this pivotal study the differences between pantoprazole 20 mg and ranitidine 150 mg results were significant; however the unpublished study conclusion for BGI022 were very similar to those of the published ranitidine 150 mg comparative study VMG306 and overall does not add significant value to the application.

- BF010 (CSR 298E/99)
  This study compared the efficacy of omeprazole 10 mg versus pantoprazole 20 mg at day 28 in patients without oesophagitis established by endoscopy. No day 14 data was available in the study report. In the non-prescription product setting, the patient would be self-referring to their physician if no symptomatic relief was obtained by day 14, making this study of limited value in the non-prescription context. Additionally, the usual starting dose for omeprazole in reflux disease is 20 mg; 10 mg omeprazole is not therapeutically equivalent to 20 mg pantoprazole. The study contained a treatment phase C; days 29-56, but again, this is not relevant to a non-prescription indication of no more than 28 days. Overall this study provides no relevant data analogous to the initial non-prescription medication period of up to 14 days. Additionally, in other studies efficacy of pantoprazole was compared to other PPIs (lansoprazole, esomeprazole) and it was found to be non-inferior to these PPIs in relieving symptoms of heartburn and acid regurgitation (Study VMG305 and M3-320).

- VMG309 (CSR 323/2004)
  This study compared the efficacy of omeprazole 10 mg versus pantoprazole 20 mg after one and two weeks or treatment. Symptomatic relief was comparable between the products though no statistically significant differences could be found between the groups at the end of week 1. No week 2 relief rate analysis was provided. The findings of this study are in line with other published studies (Study VMG305 and M3-320), which showed that the efficacy of pantoprazole is non-inferior to other PPIs (such as lansoprazole and esomeprazole).

- ESP009 (CSR 396/2004)
  This study compared the efficacy of 20 mg pantoprazole once daily with 150 mg twice daily ranitidine in healing of oesophagitis and freedom from GORD symptoms after treatment. Pantoprazole was superior to ranitidine in the treatment of key GORD symptoms. Similar results were shown by study FK3059, VMG306, FK3034, BGSA006, which also showed superiority of 20 mg pantoprazole compared to 300 mg ranitidine in the treatment of reflux symptoms.

- MEX020 (CSR 200/2004)
  In this study the efficacy of 20 mg pantoprazole was compared to 10 mg omeprazole at day 28 in

patients with reflux oesophagitis. The study concluded that pantoprazole 20 mg has a trend to have a faster relief of symptoms during the first 7 days of treatment compared with omeprazole 10 mg, but no statistically significant differences were found after 7 days, 4 weeks or 8 weeks treatment between the groups. 14 day data was not provided by this study. The shortcomings of this study are the same as described above for study BF010: lack of day 14 makes this study of limited value in the non-prescription context where the patient would be self-referring to their physician if no symptomatic relief was obtained by day 14. The usual starting dose for omeprazole in reflux disease is 20 mg; 10 mg omeprazole is not therapeutically equivalent to 20 mg pantoprazole. Additionally, in other studies efficacy of pantoprazole was compared to other PPIs (lansoprazole, esomeprazole) and it was found to be non-inferior to these PPIs in relieving symptoms of heartburn and acid regurgitation (Study VMG305 and M3-320).

- FK3037 (CSR 105/96)
  This study compared the efficacy and tolerability of pantoprazole 20 mg, 40 mg, or 80 mg in healing of oesophagitis and freedom from GORD symptoms. The results showed that all of the above doses are effective and comparable in the treatment of GORD. Similar results were shown in the published study M3-316 which compared the efficacy of 20 and 40 mg pantoprazole in the treatment of GORD symptoms.

Whereas:

- to support clinical efficacy and safety, the application is based on the results of 17 clinical studies. None of the 6 above-mentioned studies provide data to support the proposed indication and treatment duration that could not be derived from the other 11 studies provided in the application. Therefore, the 6 above-mentioned studies do not provide clinical data which has genuine impact on the assessment of the application.

the CHMP concluded that the studies BY1023/BGI022, BY1023/BF010, BY1023/ESP009, BY1023/MEX020, BY1023/FK3037 and BY1023/VMG309 submitted by the applicant for which the claim of one year data exclusivity is sought, were not relevant and necessary to the classification of SOMAC Control 20 mg gastro-resistant tablets as ‘medicinal product not subject to medical prescription’.