Public Assessment Report

Decentralised Procedure

Pantoprazole 40mg Powder for Solution for Injection

UK/H/1592/001/DC

UK licence no: PL 11204/0213

STADA Arzneimittel AG
LAY SUMMARY

On the 27th September, the Medicine and Healthcare products Regulatory Agency (MHRA) granted STADA Arzneimittel AG a Marketing Authorisation (licence) for the medicinal product Pantoprazole 40mg powder for injection (PL 11204/0213). This licence was granted via the decentralised procedure (UK/H/1592/001/DC), with the UK as the Reference Member State (RMS) and Austria, Belgium, Denmark, Luxembourg, The Netherlands, Norway, Poland, Romania, Sweden and Slovenia as Concerned Member States (CMS).

Pantoprazole is a selective ‘proton pump inhibitor’ a medicine which reduces the amount of acid produced in the stomach. It is used for treating related diseases of the stomach and intestine such as reflux oesophagitis (inflammation of the tube that connects the throat to the stomach); stomach and intestinal ulcers and Zollinger-Ellison-Syndrome and other conditions that produce too much acid in the stomach. 

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of taking Pantoprazole 40mg powder for injection outweigh the risks; hence a Marketing Authorisation has been granted.
<table>
<thead>
<tr>
<th>Module</th>
<th>Description</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Introduction</td>
<td>23</td>
</tr>
<tr>
<td>2</td>
<td>Quality aspects</td>
<td>25</td>
</tr>
<tr>
<td>3</td>
<td>Pre-clinical aspects</td>
<td>28</td>
</tr>
<tr>
<td>4</td>
<td>Clinical aspects</td>
<td>28</td>
</tr>
<tr>
<td>5</td>
<td>Scientific Discussion</td>
<td>23</td>
</tr>
<tr>
<td>6</td>
<td>Steps taken after initial procedure</td>
<td>31</td>
</tr>
</tbody>
</table>

**TABLE OF CONTENTS**

Module 1: Information about initial procedure   Page 4
Module 2: Summary of Product Characteristics   Page 5
Module 3: Product Information Leaflets          Page 13
Module 4: Labelling                             Page 20
Module 5: Scientific Discussion                 Page 23
Module 6: Steps taken after initial procedure   Page 31
## Module 1

<table>
<thead>
<tr>
<th><strong>Product Name</strong></th>
<th>Pantoprazole 40mg powder for solution for injection</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of Application</strong></td>
<td>Generic, Article 10.1</td>
</tr>
<tr>
<td><strong>Active Substance</strong></td>
<td>Pantoprazole Sodium Sesquihydrate</td>
</tr>
<tr>
<td><strong>Form</strong></td>
<td>Powder for solution for injection</td>
</tr>
<tr>
<td><strong>Strength</strong></td>
<td>40mg</td>
</tr>
</tbody>
</table>
| **Marketing Authorisation Holder** | STADA ARZNEIMITTEL AG  
Stadastrasse 2-18  
Bad Vilbel  
D-61118  
Germany |
| **Reference Member State (RMS)** | UK |
| **Concerned Member State (CMS)** | Austria, Belgium, Denmark, Luxembourg, The Netherlands, Norway, Poland, Romania, Sweden and Slovenia |
| **Procedure Number** | UK/H/1592/001/DC |
| **End of Procedure** | 25th August 2010 |
Module 2
SUMMARY OF PRODUCT CHARACTERISTICS

The UK Summary of Product Characteristics (SmPC) for Pantoprazole 40mg powder for solution for injection (PL 11204/0213) is as follows:

1 NAME OF THE MEDICINAL PRODUCT
Pantoprazole 40 mg powder for solution for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
One vial contains 40 mg of pantoprazole (as pantoprazole sodium sesquihydrate).

Excipients
Each vial contains 0 – 0.150 mg sodium hydroxide.
This medicinal product contains less than 1 mmol sodium (23 mg) per vial, i.e. is essentially ‘sodium-free’.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Powder for solution for injection. White to off-white powder.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
- Reflux oesophagitis.
- Gastric and duodenal ulcer.
- Zollinger-Ellison-Syndrome and other pathological hypersecretory conditions.

4.2 Posology and method of administration
This medicine should be administered by a healthcare professional and under appropriate medical supervision.

Intravenous administration of pantoprazole is recommended only if oral administration is not appropriate. Data are available on intravenous use for up to 7 days. Therefore, as soon as oral therapy is possible, treatment with pantoprazole i.v. should be discontinued and 40 mg pantoprazole p.o. should be administered instead.

Recommended dose
Gastric and duodenal ulcer, reflux oesophagitis
The recommended intravenous dose is one vial of Pantoprazole 40 mg powder for solution for injection (40 mg pantoprazole) per day.

Zollinger-Ellison-Syndrome and other pathological hypersecretory conditions
For the long-term management of Zollinger-Ellison-Syndrome and other pathological hypersecretory conditions patients should start their treatment with a daily dose of 80 mg pantoprazole i.v. Thereafter, the dose can be titrated up or down as needed using measurements of gastric acid secretion to guide. With doses above 80 mg daily, the dose should be divided and given twice daily. A temporary increase of the dose above 160 mg pantoprazole is possible but should not be applied longer than required for adequate acid control. In case a rapid acid control is required, a starting dose of 2 x 80 mg pantoprazole i.v. is sufficient to manage a decrease of acid output into the target range (<10 mEq/h) within one hour in the majority of patients.

Special populations
Paediatric patients
The experience in children is limited. Therefore, Pantoprazole 40 mg powder for solution for injection is not recommended for use in patients below 18 years of age until further data become available.

Hepatic Impairment
A daily dose of 20 mg pantoprazole (half a vial of 40 mg pantoprazole) should not be exceeded in patients with severe liver impairment (see section 4.4).
Renal Impairment
No dose adjustment is necessary in patients with impaired renal function.

Elderly
No dose adjustment is necessary in elderly patients.

Method of administration
A ready-to-use solution is prepared in 10 ml of sodium chloride 9 mg/ml (0.9 %) solution for injection.
For instructions for preparation see section 6.6. The prepared solution may be administered directly or may be administered after mixing it with 100 ml sodium chloride 9 mg/ml (0.9 %) solution for injection or glucose 55 mg/ml (5 %) solution for injection.

After preparation the solution must be used within 12 hours.

The medicinal product should be administered intravenously over 2 - 15 minutes.

4.3 Contraindications
Hypersensitivity to the active substance, substituted benzimidazoles, or to any of the excipients.

4.4 Special warnings and precautions for use

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

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

Hepatic Impairment
In patients with severe liver impairment, the liver enzymes should be monitored during therapy. In the case of a rise of the liver enzymes, the treatment should be discontinued (see section 4.2).

Co-administration with atazanavir
Co-administration of atazanavir with proton pump inhibitors is not recommended (see section 4.5). If the combination of atazanavir with a proton pump inhibitor is judged unavoidable, close clinical monitoring (e.g virus load) is recommended in combination with an increase in the dose of atazanavir to 400 mg with 100 mg of ritonavir. A pantoprazole dose of 20 mg per day should not be exceeded.

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

Sodium
This medicinal product contains less than 1 mmol sodium (23 mg) per vial, i.e. is essentially ‘sodium-free’.

4.5 Interaction with other medicinal products and other forms of interaction

Effect of pantoprazole on the absorption of other medicinal products
Because of profound and long lasting inhibition of gastric acid secretion, pantoprazole may reduce the absorption of drugs with a gastric pH dependent bioavailability, e.g some azole antifungals as ketoconazole, itraconazole, posaconazole and other medicine as erlotinib.

HIV medications (atazanavir)
Co-administration of atazanavir and other HIV medications whose absorption is pH-dependent with proton-pump inhibitors might result in a substantial reduction in the bioavailability of these HIV medications and might impact the efficacy of these medicines. Therefore, the co-administration of proton pump inhibitors with atazanavir is not recommended (see section 4.4).

Coumarin anticoagulants (phenprocoumon or warfarin)
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 I INR is recommended after initiation, termination or during irregular use of pantoprazole.

Other interactions studies
Pantoprazole is extensively metabolized in the liver via the cytochrome P450 enzyme system. The main metabolic pathway is demethylation by CYP2C19 and other metabolic pathways include oxidation by CYP3A4. Interaction studies with drugs also metabolized with these pathways, like carbamazepine, diazepam, glibenclamide, nifedipine, and an oral contraceptive containing levonorgestrel and ethinyl oestradiol did not reveal clinically significant interactions.

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

There were no interactions with concomitantly administered antacids.

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

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 (see section 5.3). The potential risk for humans is unknown. Pantoprazole should not be used during pregnancy unless clearly necessary.

Lactation
Animal studies have shown excretion of pantoprazole in breast milk. Excretion into human milk has been reported. Therefore a decision on whether to continue/discontinue breast-feeding or to continue/discontinue therapy with pantoprazole should be made taking into account the benefit of breast-feeding to the child and the benefit of pantoprazole therapy to women.

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 occurring in approximately 1 % of patients.

The table below lists adverse reactions reported with pantoprazole, 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).

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

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.
Table 1. Adverse reactions with pantoprazole in clinical trials and post-marketing experience

<table>
<thead>
<tr>
<th>Frequency</th>
<th>System</th>
<th>Organ Class</th>
<th>Common</th>
<th>Uncommon</th>
<th>Rare</th>
<th>Very rare</th>
<th>Not known</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Blood and lymphatic system disorders</td>
<td></td>
<td></td>
<td></td>
<td>Thrombocytopenia; Leukopenia</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Immune system disorders</td>
<td></td>
<td></td>
<td>Hypersensitivity (including anaphylactic reactions and anaphylactic shock)</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Metabolism and nutrition disorders</td>
<td></td>
<td>Hyper-lipidaemias and lipid increases (triglycerides, cholesterol); Weight changes</td>
<td>Hypo-natraemia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Psychiatric disorders</td>
<td>Sleep disorders</td>
<td>Depression (and all aggravations)</td>
<td>Disorien-tation (and all aggravations)</td>
<td>Hallucination; Confusion (especially in pre-disposed patients, as well as the aggravation of these symptoms in case of pre-existence)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Nervous system disorders</td>
<td>Headache; Dizziness</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Eye disorders</td>
<td></td>
<td>Disturbances in vision / blurred vision</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>Gastrointestinal disorders</td>
<td>Diarrhoea; Nausea / vomiting; Abdominal distension and bloating; Constipation; Dry mouth; Abdominal pain and discomfort</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hepatobiliary disorders</td>
<td>Liver enzymes increased (transaminases, γ-GT)</td>
<td>Bilirubin increased</td>
<td>Hepatocellular injury; Jaundice; Hepatocellular failure</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### 4.9 Overdose

There are no known symptoms of overdose in man. Systemic exposure with up to 240 mg administered intravenously over 2 minutes were well tolerated. As pantoprazole is extensively protein bound, it is not readily dialysable.

In the case of 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 in the acidic environment in the parietal cells where it inhibits the H⁺, K⁺-ATPase enzyme, i.e. the final stage in the production of hydrochloric acid in the stomach. The inhibition is dose-dependent and affects both basal and stimulated acid secretion. In most patients, freedom from symptoms is achieved within 2 weeks. As with other proton pump inhibitors and H2 receptor inhibitors, treatment with pantoprazole reduces acidity in the stomach and thereby increases gastrin in proportion to the reduction in acidity. The increase in gastrin is reversible. Since pantoprazole binds to the enzyme distal to the cell receptor level, it can inhibit hydrochloric acid secretion independently of stimulation by other substances (acetylcholine, histamine, gastrin). The effect is the same whether the product is given orally or intravenously.

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

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<table>
<thead>
<tr>
<th>Skin and subcutaneous tissue disorders</th>
<th>Rash / exanthema / eruption; Pruritus</th>
<th>Urticaria; Angioedema</th>
<th>Stevens-Johnson syndrome; Lyell syndrome; Erythema multiforme; Photo-sensitivity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Musculoskeletal and connective tissue disorders</td>
<td>Arthralgia; Myalgia</td>
<td></td>
<td></td>
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<tr>
<td>Renal and urinary disorders</td>
<td></td>
<td></td>
<td>Interstitial nephritis</td>
</tr>
<tr>
<td>Reproductive system and breast disorders</td>
<td></td>
<td>Gynaecomastia</td>
<td></td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
<td>Injection site thrombophlebitis</td>
<td>Asthenia, fatigue and malaise</td>
<td>Body temperature increased; Oedema peripheral</td>
</tr>
</tbody>
</table>
5.2 Pharmacokinetic properties

General pharmacokinetics
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.

Distribution
Pantoprazole’s serum protein binding is about 98 %. Volume of distribution is about 0.15 l/kg

Elimination
The substance is almost exclusively metabolized in the liver. The main metabolic pathway is demethylation by CYP2C19 with subsequent sulphate conjugation, other metabolic pathway include oxidation by CYP3A4. Terminal half-life is about 1 hour and clearance is about 0.1 l/h/kg. There were a few cases of subjects with delayed elimination. Because of the specific binding of pantoprazole to the proton pumps of the parietal cell the elimination half-life does not correlate with the much longer duration of action (inhibition of acid secretion). Renal elimination represents the major route of excretion (about 80 %) for the metabolites of pantoprazole, the rest is excreted with the faeces. The main metabolite in both the serum and urine is desmethylpantoprazole which is conjugated with sulphate. The half-life of the main metabolite (about 1.5 hours) is not much longer than that of pantoprazole.

Characteristics in patients/special groups of subjects
Approximately 3 % of the European population lack a functional CYP2C19 enzyme and are called poor metabolisers. In these individuals the metabolism of pantoprazole is probably mainly catalysed by CYP3A4. After a single-dose administration of 40 mg pantoprazole, the mean area under the plasma concentration-time curve was approximately 6 times higher in poor metabolisers than in subjects having a functional CYP2C19 enzyme (extensive metabolisers). Mean peak plasma concentrations were increased by about 60 %. These findings have no implications for the posology of pantoprazole.

No dose reduction is recommended when pantoprazole is administered to patients with impaired renal function (incl. dialysis patients). As with healthy subjects, pantoprazole’s half-life is short. Only very small amounts of pantoprazole are dialyzed. Although the main metabolite has a moderately delayed half-life (2 – 3 h), excretion is still rapid and thus accumulation does not occur. Although for patients with liver cirrhosis (classes A and B according to Child) the half-life values increased to between 7 and 9 h and the AUC values increased by a factor of 5 – 7, the maximum serum concentration only increased slightly by a factor of 1.5 compared with healthy subjects.

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

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

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

In the two-year carcinogenicity studies in rats neuroendocrine neoplasms were found. In addition, squamous cell papillomas were found in the forestomach of rats. The mechanism leading to the formation of gastric carcinoids by substituted benzimidazoles has been carefully investigated and allows the conclusion that it is a secondary reaction to the massively elevated serum gastrin levels occurring in the rat during chronic high-dose treatment. In the two-year rodent studies an increased number of liver tumors was observed in rats 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). The occurrence of these neoplasms is associated with the pantoprazole-induced changes in the breakdown of thyroxine in the rat liver. As the therapeutic dose in man is low, no harmful effects on the thyroid glands are expected.
In animal reproduction studies, signs of slight fetotoxicity were observed at doses above 5 mg/kg. 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
Sodium hydroxide (for pH adjustment)

6.2 Incompatibilities
This medicinal product must not be mixed with other medicinal products except those mentioned in section 6.6.

6.3 Shelf life
Unopened vial: 12 months
After reconstitution, or reconstitution and dilution, chemical and physical in use stability has been demonstrated for 12 hours at 25 °C.
From a microbiological point of view, the product should be used immediately.
If not used immediately, in-use storage times and conditions are the responsibility of the user.

6.4 Special precautions for storage
Do not store above 25 °C.
Keep the vial in the outer carton in order to protect from light.

For storage conditions of the reconstituted and diluted medicinal product see section 6.3.

6.5 Nature and contents of container
15 ml clear colourless glass vial type I (Ph. Eur.), closed with grey rubber stopper, an aluminium seal and a white flip-off cap.
 Packs of 1, 5 and 10 vials.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal
A ready-to-use solution is prepared by injecting 10 ml of sodium chloride 9 mg/ml (0.9 %) solution for injection into the vial containing the powder. The appearance of the product after reconstitution is a clear yellowish solution. This solution may be administered directly or may be administered after mixing it with 100 ml sodium chloride 9 mg/ml (0.9 %) solution for injection or glucose 55 mg/ml (5 %) solution for injection. Glass or plastic containers should be used for dilution.

After reconstitution, or reconstitution and dilution, chemical and physical in use stability has been demonstrated for 12 hours at 25 °C. From a microbiological point of view, the product should be used immediately. Pantoprazole powder for solution for injection should not be prepared or mixed with solvents other than those stated.

The medicine should be administered intravenously over 2-15 minutes.

The contents of the vial are for single use only. Any product that has remained in the container or the visual appearance of which has changed (e.g. if cloudiness or precipitation is observed) should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER
STADA ARZNEIMITTEL AG
Stadastrasse 2-18
Bad Vilbel
D-61118
Germany

8 MARKETING AUTHORISATION NUMBER(S)
PL 11204/0213

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
Module 3
Product Information Leaflet

PACKAGE LEAFLET: INFORMATION FOR THE USER

Pantoprazole 40 mg powder for solution for injection

Pantoprazole

Read all of this leaflet carefully before you start using this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

In this leaflet:
1. WHAT PANTOPRAZOLE 40 MG POWDER FOR SOLUTION FOR INJECTION IS AND WHAT IT IS USED FOR
2. BEFORE YOU USE PANTOPRAZOLE 40 MG POWDER FOR SOLUTION FOR INJECTION

1. WHAT PANTOPRAZOLE 40 MG POWDER FOR SOLUTION FOR INJECTION IS AND WHAT IT IS USED FOR

Pantoprazole 40 mg powder for solution for injection is a selective “proton pump inhibitor”, a medicine which reduces the amount of acid produced in your stomach. It is used for treating acid-related diseases of the stomach and intestine.

This preparation is injected into a vein and will only be given to you if your doctor thinks pantoprazole injections are more suitable for you at the moment than pantoprazole tablets. Tablets will replace your injections as soon as your doctor sees fit.

Pantoprazole 40 mg powder for solution for injection is used for treating:

- Reflux oesophagitis. An inflammation of your oesophagus (the tube which connects your throat to your stomach) accompanied by the regurgitation of stomach acid.

- Stomach and duodenal ulcers.

- Zollinger-Ellison-Syndrome and other conditions producing too much acid in the stomach

2. BEFORE YOU USE PANTOPRAZOLE 40 MG POWDER FOR SOLUTION FOR INJECTION

Do not use Pantoprazole 40 mg powder for solution for injection
- If you are allergic (hypersensitive) to pantoprazole or any of the other ingredients of Pantoprazole 40 mg powder for solution for injection (see section 6).
If you are allergic to medicines containing other proton pump inhibitors.

**Take special care with** Pantoprazole 40 mg powder for solution for injection

- If you have severe liver problems. Please tell your doctor if you ever had problems with your liver in the past. He will check your liver enzymes more frequently. In the case of a rise of liver enzymes the treatment should be stopped.
- If you are taking a medicine containing atazanavir (for the treatment of HIV-infection) at the same time as pantoprazole, ask your doctor for specific advice.

**Tell your doctor immediately** if you notice any of the following symptoms:

- an unintentional loss of weight
- repeated vomiting
- difficulty in swallowing
- vomiting blood
- you look pale and feel weak (anaemia)
- you notice blood in your stools
- severe and/or persistent diarrhoea, as Pantoprazole 40 mg powder for solution for injection has been associated with a small increase in infectious diarrhoea.

Your doctor may decide that you need some tests to rule out malignant disease because pantoprazole also alleviates the symptoms of cancer and could cause delay in diagnosing it. If your symptoms continue in spite of your treatment, further investigations will be considered.

**Taking other medicines**

Pantoprazole 40 mg powder for solution for injection injections may influence the effectiveness of other medicines, so tell your doctor if you are taking

- Medicines such as ketoconazole, itraconazole and posaconazole (used to treat fungal infections) or crlominb (used for certain types of cancer) because Pantoprazole 40 mg powder for solution for injection may stop these and other medicines from working properly.
- Warfarin and phenprocoumon, which affect the thickening or thinning of the blood. You may need further checks.
- Atazanavir (used to treat HIV-infection).

Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

**Pregnancy and breast-feeding**

There are no adequate data from the use of pantoprazole in pregnant women. Excretion into human milk has been reported. If you are pregnant, or think you may be pregnant, or if you are breastfeeding, you should use this medicine only if your doctor considers the benefit for you greater than the potential risk for your unborn child or baby.

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
Important information about some of the ingredients of Pantoprazole 40 mg powder for solution for injection
This medicine contains less than 1 mmol sodium (23 mg) per vial, i.e. is essentially ‘sodium-free’.

3. HOW TO USE PANTOPRAZOLE 40 MG POWDER FOR SOLUTION FOR INJECTION

Your nurse or your doctor will administer the daily dose to you as an injection into a vein over a period of
2 - 15 minutes.

The usual dose is:
For gastric ulcers, duodenal ulcers and reflux oesophagitis.
One vial (40 mg pantoprazole) a day.

For the long-term treatment of Zollinger-Ellison syndrome and other conditions in which too much stomach acid is produced.
Two vials (80 mg pantoprazole) a day.

Your doctor may later adjust the dose, depending on the amount of stomach acid you produce. If you are prescribed more than two vials (80 mg) a day, the injections will be given in two equal doses.
Your doctor may prescribe a temporary dose of more than four vials (160 mg) a day. If your stomach acid level needs
to be controlled rapidly, a starting dose of 160 mg (four vials) should be enough to lower the
amount of stomach acid sufficiently.

Special patient groups:
- If you suffer from severe liver problems, the daily injection should be only 20 mg (half a vial).
- Children (under 18 years). These injections are not recommended for use in children.

If you use more Pantoprazole 40 mg powder for solution for injection than you should
These doses are carefully checked by your nurse or your doctor so an overdose is extremely unlikely. There are no known symptoms of overdose.

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

4. POSSIBLE SIDE EFFECTS

Like all medicines, Pantoprazole 40 mg powder for solution for injection can cause side effects, although not everybody gets them.

The frequency of possible side effects listed below is defined using the following convention:
very common (affects more than 1 user
If you get any of the following side effects, tell your doctor immediately, or contact the casualty department at your nearest hospital:

- **Serious allergic reactions (frequency rare):** swelling of the tongue and/or throat, difficulty in swallowing, hives ( acne rash), difficulties in breathing, allergic facial swelling (Quincke’s oedema/angioedema), severe dizziness with very fast heartbeat and heavy sweating.

- **Serious skin conditions (frequency not known):** blistering of the skin and rapid deterioration of your general condition, erosion (including slight bleeding) of eyes, nose, mouth/lips or genitals (Stevens-Johnson Syndrome, Lyell Syndrome, Erythema multiforme) and sensitivity to light.

- **Other serious conditions (frequency not known):** yellowing of the skin or whites of the eyes (severe damage to liver cells, jaundice) or fever, rash, and enlarged kidneys sometimes with painful urination and lower back pain (serious inflammation of the kidneys).

**Other side effects are:**

- **Common** (affects 1 to 10 users in 100)
  - inflammation of the wall of the vein and blood clotting (thrombophlebitis) where the medicine is injected.

- **Uncommon** (affects 1 to 10 users in 1,000)
  - headache; dizziness; diarrhoea; feeling sick; vomiting; bloating and flatulence (wind); constipation; dry mouth; abdominal pain and discomfort; skin rash, exanthema, eruption; itching, feeling weak, exhausted or generally unwell; sleep disorders.

- **Rare** (affects 1 to 10 users in 10,000)
  - disturbances in vision such as blurred vision; hives; pain in the joints; muscle pains; weight changes; raised body temperature; swelling of the extremities (peripheral oedema); allergic reactions; depression; breast enlargement in males.

- **Very Rare** (affects less than 1 user in 10,000)
  - disorientation.

  - **Not known** (frequency cannot be estimated from the available data)
    - Hallucination, confusion (especially in patients with a history of these symptoms); decreased sodium level in blood.

**Side effects identified through blood tests:**

- **Uncommon** (affects 1 to 10 users in 1,000)
  - an increase in liver enzymes.

- **Rare** (affect 1 to 10 users in 10,000)
  - an increase in bilirubin; increased fats in the blood.

- **Very Rare** (affects less than 1 user in 10,000)
  - a reduction in the number of blood platelets, which may cause you to bleed or bruise.
more than normal; a reduction in the number of white blood cells, which may lead to
more frequent infections.

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 PANTOPRAZOLE 40 MG POWDER FOR SOLUTION FOR INJECTION

Keep out of the reach and sight of children.

Do not use Pantoprazole 40 mg powder for solution for injection after the expiry date,
which is stated on the carton and the vial after EXP. The expiry date refers to the last
day of that month.

Do not store above 25 °C.
Keep the vial in the outer carton in order to protect it from light.

Use the reconstituted solution within 12 hours.
Use the reconstituted and diluted solution within 12 hours.

From a microbiological point of view, the product should be used immediately. If not used
immediately, in-use storage times and conditions prior to use are the responsibility of the user and
would normally not be longer than 12 hours at not more than 25 °C.

Do not use Pantoprazole 40 mg powder for solution for injection if you notice that the
visual appearance has changed (e.g. if cloudiness or precipitation is observed).

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 Pantoprazole 40 mg powder for solution for injection contains

- The active substance is pantoprazole. Each vial contains 40 mg of pantoprazole (as sodium sequihydrate).
- The other ingredients is sodium hydroxide (for pH adjustment).

What Pantoprazole 40 mg powder for solution for injection looks like and contents of the pack

Pantoprazole 40 mg powder for solution for injection is a white to off-white powder for solution for injection. It comes in a 10 ml clear glass vial closed with an aluminium cap and grey rubber stopper containing 40 mg powder for solution for injection.

Pantoprazole 40 mg powder for solution for injection is available in the following pack sizes:

Pack with 1 vial.
Pack with 5 (5x1) vials.
Pack with 10 (10x1) vials.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

[To be completed nationally]
{Name and address}
&lt{tel}&gt
&lt{fax}&gt
&lt{e-mail}&gt

Manufacturer

[To be completed nationally]
{Name and address}
&lt{tel}&gt
&lt{fax}&gt
&lt{e-mail}&gt
The following information is intended for medical or healthcare professionals only:

A ready-to-use solution is prepared by injecting 10 ml of sodium chloride 9 mg/ml (0.9 %) solution for injection into the vial containing the dry powder. This solution may either be administered directly or after mixing it with 100 ml sodium chloride 9 mg/ml (0.9 %) solution for injection or glucose 55 mg/ml (5 %) solution for injection. Glass or plastic containers should be used for dilution.

Pantoprazole 40 mg powder for solution for injection should not be prepared or mixed with solvents other than those stated.

After preparation, the solution must be used within 12 hours. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 12 hours, at no more than 25 °C.

The medicine should be administered intravenously over 2 - 15 minutes.

The content of the vial is for single intravenous use only. Any product that has remained in the container or whose visual appearance has changed (e.g. if cloudiness or precipitation is observed) must be discarded.
Module 4
Labelling

Carton

<table>
<thead>
<tr>
<th>PARTICULARS TO APPEAR ON THE OUTER PACKAGING</th>
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<tr>
<td>Carton box</td>
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</table>

1. **NAME OF THE MEDICINAL PRODUCT**

   [Pantoprazole] 40 mg powder for solution for injection

   Pantoprazole

2. **STATEMENT OF ACTIVE SUBSTANCE(S)**

   Each vial contains 40 mg pantoprazole (as pantoprazole sodium sesquihydrate).

3. **LIST OF EXCIPIENTS**

   Each vial contains 0 – 0.150 mg sodium hydroxide. See the package leaflet for further information.

4. **PHARMACEUTICAL FORM AND CONTENTS**

   Powder for solution for injection.

   - Pack with 1 vial
   - Pack with 5 (5x1) vials
   - Pack with 10 (10x1) 10 vials

5. **METHOD AND ROUTE(S) OF ADMINISTRATION**

   Intravenous use.
   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**
<table>
<thead>
<tr>
<th>8.</th>
<th>EXPIRY DATE</th>
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<tbody>
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<td>EXP</td>
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| Shelf life after reconstitution (and dilution): 12 hours

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<th>SPECIAL STORAGE CONDITIONS</th>
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<tr>
<td>Do not store above 25°C.</td>
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<td>Keep the vial in the outer carton in order to protect from light.</td>
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<th>10.</th>
<th>SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE</th>
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<tr>
<th>11.</th>
<th>NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER</th>
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<tbody>
<tr>
<td>ALFRED E. TIEFENBACHER (GmbH &amp; Co. KG), Van-der-Smissen-Strasse 1, 22767 Hamburg, Germany.</td>
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<th>14.</th>
<th>GENERAL CLASSIFICATION FOR SUPPLY</th>
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<th>15.</th>
<th>INSTRUCTIONS ON USE</th>
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<th>16.</th>
<th>INFORMATION IN BRAILLE</th>
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<td>&lt;Justification for not including Braille accepted-&gt;</td>
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</table>
**Label**

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<tr>
<th>PARTICULARS TO APPEAR ON THE IMMEDIATE PACKAGING</th>
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<tbody>
<tr>
<td>Vial Label</td>
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</tbody>
</table>

1. **NAME OF THE MEDICINAL PRODUCT**

   [Pantoprazole] 40 mg powder for solution for injection

   Pantoprazole

2. **STATEMENT OF ACTIVE SUBSTANCE(S)**

   Each vial contains 40 mg pantoprazole (as sodium sesquihydrate).

3. **METHOD AND ROUTE(S) OF ADMINISTRATION**

   For intravenous use.

4. **EXPIRY DATE**

   EXP
   Shelf life after reconstitution: 12 hours

5. **SPECIAL STORAGE CONDITIONS**

   Do not store above 25°C.
   Keep the vial in the outer carton in order to protect from light.

6. **BATCH NUMBER**

   Batch
Module 5

Scientific discussion during initial procedure

I  INTRODUCTION

On 25th August 2010, Germany and the UK agreed to grant a Marketing Authorisation (MA) to STADA ARZNEIMITTEL AG for the medicinal product Pantoprazole 40mg powder for injection. The MA was granted via a Decentralised Procedure (DCP), with the UK as Reference Member State (RMS UK/H/1592/001/DC). After the national phase, an MA was granted in the UK on 27th September 2010 (PL 11204/0213).

This application was made under Article 10.1 of Directive 2001/83/EC for Pantoprazole 40mg powder for injection, containing the known active substance pantoprazole sodium sesquihydrate. The reference medicinal product for this application is Protium® 40mg i.v (PL 20141/0003), licensed on the 1st April 2003 to Altana Pharma AG which subsequently underwent a change of ownership and is currently licensed to Nycomed GmbH.

Pantoprazole is a proton pump inhibitor, i.e. it inhibits specifically and dose-proportionally the gastric H⁺/K⁺-ATPase enzyme, which is responsible for acid secretion in the parietal cells of the stomach.

It is used for the treatment of acid related disease like upper gastrointestinal ulceration and oesophageal reflux disease and – in conjunction with antibiotics – for the eradication of Helicobacter pylori.

No new preclinical or clinical efficacy studies were conducted for this application, which is acceptable given that the application was for a generic version of product that has been licensed for over 10 years. A bioequivalence study is not necessary to support this application for a parenteral product.

The RMS has been assured that acceptable standards of Good Manufacturing Practice (GMP) are in place for these product types at all sites responsible for the manufacture and assembly of these products. Evidence of compliance with GMP has been provided for the named manufacturing and assembly sites. For manufacturing sites within the Community, the RMS has accepted copies of current manufacturer authorisations issued by inspection services of the competent authorities as certification that acceptable standards of GMP are in place at those sites.

For manufacturing sites outside the community, the RMS has accepted copies of current GMP certificates or satisfactory inspection summary reports, ‘close-out letters’ or ‘exchange of information’ issued by the inspection services of the competent authorities (or those countries with which the EEA has a Mutual Recognition Agreement for their own territories) as certification that acceptable standards of GMP are in place at those non-Community sites.

The RMS considers that the pharmacovigilance system, as described by the MAH, fulfils the requirements and provides adequate evidence that the MAH has the services of a qualified person responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country. The Marketing Authorisation Holder has provided adequate justification for not submitting a Risk Management Plan (RMP). As the application is for a generic version of an already authorised reference product, for which safety concerns requiring additional risk minimisation have not been identified, a risk minimisation system is not considered
necessary. The reference product has been in use for many years and the safety profile of the active is well established.

The Marketing Authorisation Holder has provided adequate justification for not submitting an Environmental Risk Assessment (ERA). This was an application for a generic product and there is no reason to conclude that marketing of this product will change the overall use pattern of the existing market.
II. ABOUT THE PRODUCT

<table>
<thead>
<tr>
<th>Name of the product in the Reference Member State</th>
<th>Pantoprazole 40 mg powder for solution for injection</th>
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</thead>
<tbody>
<tr>
<td>Name(s) of the active substance(s) (INN)</td>
<td>Pantoprazole Sodium Sesquihydrate</td>
</tr>
<tr>
<td>Pharmacotherapeutic classification (ATC code)</td>
<td>Proton pump inhibitors A02BC02</td>
</tr>
<tr>
<td>Pharmaceutical form and strength(s)</td>
<td>Powder for solution for injection 40mg</td>
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<tr>
<td>Reference numbers for the Decentralised Procedure</td>
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<tr>
<td>Reference Member State</td>
<td>United Kingdom</td>
</tr>
<tr>
<td>Member States concerned</td>
<td>Austria, Belgium, Denmark, Luxembourg, The Netherlands, Norway, Poland, Romania, Sweden and Slovenia</td>
</tr>
<tr>
<td>Marketing Authorisation Number(s)</td>
<td>PL 11204/0213</td>
</tr>
<tr>
<td>Name and address of the authorisation holder</td>
<td>STADA ARZNEIMITTEL AG Stadastrasse 2-18 Bad Vilbel D-61118 Germany</td>
</tr>
</tbody>
</table>

III. SCIENTIFIC OVERVIEW AND DISCUSSION

III.1 QUALITY ASPECTS

DRUG SUBSTANCE

INN: Pantoprazole sodium sesquihydrate

Structure:

```
INN     Pantoprazole sodium sesquihydrate
Structure:

Molecular formula: C_{16}H_{14}F_{2}N_{3}NaO_{4}S. 3/2H_{2}O
Molecular weight: 432.38

General Properties
Description: White or off-white powder.
Solubility: Freely soluble in water, methanol and ethanol. Practically insoluble in methylene dichloride and chloroform.

Manufacture
Synthesis of the drug substance from the designated starting materials has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specification tests are in place for all starting materials and reagents and these are supported by relevant certificates of analysis.
An appropriate specification is provided for the active substance. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications.

Appropriate proof-of-structure data have been supplied for the active substance. All potential known impurities have been identified and characterised. Satisfactory certificates of analysis have been provided for all working standards. Batch analysis data are provided and comply with the proposed specification.

The active substance is stored in appropriate packaging. Specifications and Certificates of Analysis have been provided for the packaging materials used. The primary packaging material in direct contact with the active substance satisfy Directive 2002/72/EC (as amended), and are suitable for contact with foodstuffs.

Appropriate stability data have been presented for the active substance stored in packaging representative of the proposed commercial packaging. These data demonstrate the stability of the active substance. A suitable re-test period has been applied when stored in the stated container closure system.

**DRUG PRODUCT**

**Description and Composition**

The finished product is presented as a white to off-white powder. One vial contains 40 mg of pantoprazole (as pantoprazole sodium sesquihydrate).

Other ingredients consist of pharmaceutical excipients, namely sodium hydroxide (for pH adjustment). An appropriate justification for the inclusion of this excipient has been provided. Sodium hydroxide shows compliance with its Ph Eur monograph. A satisfactory Certificate of Analysis for sodium hydroxide has been provided. The applicant has provided a declaration confirming that there are no materials of human or animal origin contained in, or used in the manufacturing process for the proposed product. Furthermore, no genetically modified organisms are used in the manufacture of the finished product.

**Pharmaceutical Development**

The aim of the pharmaceutical development programme was to produce a stable, robust, reproducible finished product that could be considered a generic medicinal product of Protium® 40mg i.v. (Nycomed GmbH). Suitable pharmaceutical development data have been provided for this application.

The physico-chemical properties of the drug product have been compared with the reference product. These data demonstrate that the proposed product can be considered a generic medicinal product of Protium® 40mg i.v. (PL 20141/0003) licensed to Nycomed GmbH).

**Impurity Profile**

Comparative impurity data were provided for the test and reference products. The impurity profiles were found to be similar, with all impurities within the specification limits.

**Manufacture**

A description and flow-chart of the manufacturing method has been provided.

Satisfactory batch formulae have been provided for the manufacture of the product, along with an appropriate account of the manufacturing process. In-process controls were
considered appropriate considering the nature of the product and the method of manufacture. Process validation studies have been conducted on three consecutive commercial batches and are acceptable.

**Finished Product Specification**

Finished product specifications are provided for both release and shelf–life, and are satisfactory; they provide an assurance of the quality and consistency of the finished product. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. Test methods have been described and adequately validated, as appropriate. Batch data are provided for three consecutive pilot-scale batches of the product, which demonstrate that the batches are compliant with the proposed release specifications. Certificates of Analysis have been provided for any reference standards used.

**Container Closure System**

The finished product is licensed for marketing in 15 ml clear colourless glass vial Type I (Ph. Eur.), closed with grey rubber stopper, an aluminium seal and a white flip-off cap. Each vial contains the equivalent to 40mg of pantoprazole. Vials are packed in units of 1, 5 and 10. The MAH has stated that not all pack sizes may be marketed and has committed to submitting mock-ups for all packaging for assessment before those pack sizes are commercially marketed. All primary product packaging complies with Directive 2002/72/EC (as amended), concerning products in contact with parenteral products.

**Stability**

Finished product stability studies have been conducted in accordance with current guidelines and results were within the proposed specification limits. Based on the results, a shelf-life of 12 months has been set, when the vial is unopened, which is satisfactory. Storage instructions are ‘Do not store above 25°C’ and ‘Keep the vial in the outer carton in order to protect from light.’

Finished product stability studies have been carried out after reconstitution as well as reconstitution and dilution. Chemical and physical in use stability has been demonstrated for 12 hours at 25°C. From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user.

**Compatibility Studies**

The stability of Pantoprazole 40mg powder for injection was studied when reconstituted initially in (0.9%) sodium chloride solution and then further diluted in 5% dextrose solution.

The stability of these solutions was monitored by determining the physiochemical parameters such as appearance of solution, pH, assay, and related substances.

The initial reconstitution of Pantoprazole 40mg powder for injection in 10ml of 0.9% sodium chloride, maintained all the physical and chemical characteristics within specification, after 12 hours at 25°C.

Dilution in 100ml 9mg/ml (0.9%) sodium chloride solution for injection or glucose 55mg/ml (5%) solution for injection, maintained all the physical and chemical characteristics within specification, after 12 hours at 25°C.
Bioequivalence Study
The product is formulated for administration as a solution by the intravenous route. Hence there is no requirement for a bioequivalence study.

Quality Overall Summary
A satisfactory quality overview is provided and has been prepared by an appropriately qualified expert. The curriculum vitae of the expert has been provided.

Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL), Labels
The SmPC, PIL and labelling are pharmaceutically acceptable.

MAA Form
The MAA form is pharmaceutically satisfactory.

Conclusion
The test product is pharmaceutically equivalent to the reference product, which has been licensed in the UK for over 10 years. Given the route of administration and pharmaceutical form, it is not necessary to perform a bioequivalence study.

There are no objections to approval of Pantoprazole 40mg powder for injection from a pharmaceutical point of view.

III.2 PRE-CLINICAL ASPECTS
The pharmacodynamic, pharmacokinetic and toxicological properties of pantoprazole are well-known. Therefore, no further studies are required and the applicant has provided none.

The pre-clinical overview was written by a suitably qualified person and is satisfactory. The curriculum vitae of the expert has been provided.

The SmPC is satisfactory from a pre-clinical viewpoint and is consistent with that for the reference product.

There are no objections to approval of Pantoprazole 40mg powder for injection from a pre-clinical point of view.

III.3 CLINICAL ASPECTS
Pharmacokinetics
No new data have been submitted and none are required for an application of this type.

Pantoprazole 40mg powder for injection is a generic version of Pantozol 40mg i.v. (Altana Pharma, Germany). The use of the reference product is well-established in the UK. Both products contain the same quantitative and qualitative composition of the active ingredient, pantoprazole.

According to CPMP guidelines, the applicant is not required to submit a bioequivalence study if the product is to be administered as an aqueous intravenous solution containing the same active substance, in the same concentration as the currently authorised product (CPMP/EWP/1401/98, subpoint 5.1.6, Parenteral solutions).
Pharmacodynamics
No new data have been submitted and none are required for an application of this type.

Clinical efficacy
No new data have been submitted and none are required for an application of this type.

Clinical safety
No new safety data have been submitted or required for this generic application. As pantoprazole is a well-known product with an acceptable adverse event profile, this is satisfactory.

Expert Report
A satisfactory clinical overview is provided, and has been prepared by an appropriately qualified physician. The curriculum vitae of the expert has been provided.

Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL), Labels
The SmPC and PIL are medically acceptable, and consistent with those for the reference product. The labelling is medically acceptable and in-line with current requirements.

MAA form
The MAA form is medically satisfactory.

Conclusion
There are no objections to approval of Pantoprazole 40mg powder for injection from a clinical point of view.
IV OVERALL CONCLUSION AND BENEFIT/RISK ASSESSMENT

QUALITY
The important quality characteristics of Pantoprazole 40mg powder for injection are well-defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

PRE-CLINICAL
No new pre-clinical data were submitted and none are required for an application of this type.

EFFICACY
The applicant’s Pantoprazole 40mg powder for injection has been demonstrated to be a generic version of the reference product Protium® 40mg i.v (Nycomed GmbH).

No new or unexpected safety concerns arise from this application.

PRODUCT LITERATURE
The SmPC and PIL are acceptable, and consistent with those for the reference product. The labelling is acceptable and in-line with current requirements.

BENEFIT/RISK ASSESSMENT
The quality of the product is acceptable, and no new preclinical or clinical safety concerns have been identified. The qualitative and quantitative assessment supports the claim that the applicant’s Pantoprazole 40mg powder for injection and the reference product Protium® 40mg i.v (Nycomed GmbH) are interchangeable. Extensive clinical experience with pantoprazole is considered to have demonstrated the therapeutic value of the active substance. The benefit/risk is, therefore, considered to be positive.
Module 6

STEPS TAKEN AFTER INITIAL PROCEDURE - SUMMARY

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