Docusign Envelope ID: E08F7841-EB08-8C41-81D7-07765DE10CF0



# PANTOLOC RANGE - PROFESSIONAL INFORMATION

## SCHEDULING STATUS

**S4**

## 1. NAME OF THE MEDICINE

**PANTOLOC® 20,** Pantoprazole sodium, Enteric-coated Tablets

**PANTOLOC® 40,** Pantoprazole sodium, Enteric-coated Tablets

**PANTOLOC® IV,** Pantoprazole sodium, Lyophilised powder for injection

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

**PANTOLOC® 20** Each tablet contains 22,6 mg pantoprazole sodium sesquihydrate equivalent to 20 mg pantoprazole and is sugar-free.

**PANTOLOC® 40** Each tablet contains 45,1 mg pantoprazole sodium sesquihydrate equivalent to 40 mg pantoprazole and is sugar-free.

**PANTOLOC® IV** Each vial contains 42,3 mg pantoprazole sodium equivalent to 40 mg pantoprazole.

Excipient with known effect (**PANTOLOC® 20,** Enteric-coated Tablets**):**

Each tablet contains 21,33 mg of mannitol and 3,40 mg sodium.

Excipient with known effect (**PANTOLOC® 40,** Enteric-coated Tablets**):**

Each tablet contains 42,70 mg of mannitol and 6,79 mg of sodium.

Excipient with known effect (**PANTOLOC® IV):**

Each vial contains 2,588 mg of sodium

For the full list of excipients, see **Section 6.1**

## 3. PHARMACEUTICAL FORM

**PANTOLOC® 20:** Yellow, oval, biconvex enteric-coated tablet with a white to off-white core, imprinted "P20" on one side.

**PANTOLOC® 40:** Yellow, oval, biconvex enteric-coated tablet, with a white to off-white core, imprinted "P40" on one side.

**PANTOLOC® IV:** A white to almost white lyophylised powder in a glass vial for intravenous injection. The reconstituted solution is a clear yellowish solution.

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## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

**PANTOLOC® IV** is indicated for intravenous administration to patients who cannot be treated orally.

**PANTOLOC® 40** and **PANTOLOC® IV** are indicated for the short-term treatment of duodenal ulcer, gastric ulcer and reflux oesophagitis.

If the duodenal ulcer has been demonstrated to be associated with *Helicobacter pylori* infection, **PANTOLOC® 40** or **PANTOLOC® IV** used in combination with appropriate antibiotics may be useful.

**PANTOLOC® 40** and **PANTOLOC® IV** are indicated for the treatment of Zollinger-Ellison Syndrome.

**PANTOLOC® 20** is indicated for the symptomatic improvement (e.g. heartburn, acid regurgitation, pain on swallowing) and healing of mild gastro-oesophageal reflux disease. In patients with healed reflux disease, recurring symptoms can be controlled using an on-demand regimen of 20 mg once daily when required.

**PANTOLOC® 20** is indicated for long-term management and prevention of relapse in gastro-oesophageal reflux disease.

**PANTOLOC® 20** is indicated for the prevention of gastroduodenal lesions and dyspeptic symptoms induced by non-selective non-steroidal anti-inflammatory drugs (NSAID's) in patients at risk, and with a need for continuous NSAID treatment.

### 4.2 Posology and method of administration

**PANTOLOC® 20** and **PANTOLOC® 40**

**PANTOLOC® 20** and **PANTOLOC® 40** should be swallowed whole with a little water either before or during breakfast.

**PANTOLOC® IV** is indicated for intravenous administration to patients who cannot be treated orally.

A ready-to-use solution is prepared by injecting 10 ml of physiological sodium chloride (0,9 %) solution into the vial containing the dry substance. **PANTOLOC® IV** may be used intravenously for up to 7 days. After preparation the solution in physiological sodium chloride solution and 5 % glucose must be used within 12 hours and any unused portion discarded after 12 hours.

The solution may be administered directly or it may be further diluted by mixing with 100 ml physiological sodium chloride solution or 5 % glucose **ONLY**. The medicine should be administered intravenously over 2 - 15 minutes.

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As soon as oral therapy is possible, treatment should be replaced with the same oral dose (**PANTOLOC® 40** tablets) in compliance with the approved dosage regimen.

**Duodenal ulcer**

The recommended oral or IV dose is **40 mg PANTOLOC®** once daily. The total treatment with intravenous and oral **PANTOLOC®** should be 2 to 4 weeks. If the duodenal ulcer has been demonstrated to be associated with *Helicobacter pylori* infection, **PANTOLOC® 40** or **PANTOLOC® IV** used in combination with appropriate antibiotics may be useful.

**Gastric ulcer**

The recommended oral or IV dose is **40 mg PANTOLOC®** once daily for 4 to 8 weeks.

In the case of a suspected gastric ulcer, malignancy of the gastric ulcer should be excluded, as treatment could conceal the symptoms and may delay diagnosis.

**Reflux oesophagitis**

The recommended oral or IV dose is **40 mg PANTOLOC®** once daily for 4 to 8 weeks.

**Zollinger-Ellison Syndrome**

For management of Zollinger-Ellison Syndrome patients should start their treatment with a daily dose of 80 mg (2 tablets of **PANTOLOC® 40** or 2 vials of **PANTOLOC® IV).** Thereafter, the dosage can be titrated up or down as needed using measurements of gastric acid secretion as a guide. With doses above 80 mg daily, the dose should be divided and given twice daily.

In case rapid acid control is required, a starting dose of 2 x 80 mg **PANTOLOC® IV** is sufficient to manage a decrease of acid output into the target range (<10 mmol/h) within one hour in the majority of patients. Transition from **PANTOLOC® IV** to the oral formulation **PANTOLOC® 40** should be performed as soon as it is clinically justified.

**Long-term treatment**

Long-term treatment with **PANTOLOC® IV** is currently not indicated as there is insufficient clinical data.

**Mild gastro-oesophageal reflux disease**

The recommended oral dose is **20 mg PANTOLOC®** per day. A 4-week period is usually required for healing of mild gastro-oesophageal reflux disease. If this is not sufficient, healing will usually be achieved within a further 4 weeks. In patients with healed reflux disease, reoccurring symptoms can be controlled using an on-demand regimen of 20 mg once daily when required.

**Long-term management and prevention of relapse in gastro-oesophageal reflux disease**

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

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

**Elderly patients**

No dosage adjustment is necessary in the elderly.

**Impaired renal and liver function**

No dosage adjustment is required in the presence of impaired renal function.

A daily dose of 20 mg **PANTOLOC®** should not be exceeded in patients with mild to moderate liver impairment (see **Section 5.2** and **Section 4.4**).

## 4.3 Contraindications

Hypersensitivity to pantoprazole.

Safety and efficacy in children have not been established.

Severely impaired liver function (**see Section 4.4**).

PANTOLOC®, should not be co-administered with nelfinavir & atazanavir (see Section 4.5).

## 4.4 Special warnings and precautions for use

**PANTOLOC® IV is for intravenous route only** and must not be given by any other route.

**PANTOLOC®** is not indicated for mild gastrointestinal complaints such as nervous dyspepsia.

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

The daily dose of 40 mg **PANTOLOC®** should not be exceeded in elderly patients or in those with impaired renal function.

***Clostridium difficile*-associated diarrhoea**

Published observational studies suggest that proton pump inhibitor therapy, like **PANTOLOC®**, may be associated with an increased risk of *Clostridium difficile*-associated diarrhoea, especially in hospitalised patients. This diagnosis should be considered for diarrhoea that does not improve **(see Section 4.8 AND Section 4.4).**

***Gastric malignancy***

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

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

***Co-administration with HIV protease inhibitors***

Co-administration of pantoprazole is not recommended with HIV protease inhibitors for which absorption is dependent on acidic intragastric pH such as atazanavir, due to significant reduction in their bioavailability (see section 4.5).

***Influence on vitamin $B_{12}$ absorption***

In patients with Zollinger-Ellison syndrome and other pathological hypersecretory conditions requiring long-term treatment, pantoprazole, as all acid-blocking medicines, may reduce the absorption of vitamin $B_{12}$ (cyanocobalamin) due to hypo- or achlorhydria. This should be considered in patients with reduced body stores or risk factors for reduced vitamin $B_{12}$ absorption on long-term therapy or if respective clinical symptoms are observed.

***Long-term treatment***

In long-term treatment, especially when exceeding a treatment period of 1 year, patients should be kept under regular surveillance.

***Gastrointestinal infections caused by bacteria***

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

***Hypomagnesaemia***

Severe hypomagnesaemia has been rarely reported in patients treated with proton pump inhibitors (PPIs) like pantoprazole for at least three months, and in most cases for a year. Serious manifestations of hypomagnesaemia such as fatigue, tetany, delirium, convulsions, dizziness, and ventricular arrhythmia can occur but they may begin insidiously and be overlooked. Hypomagnesaemia may lead to hypocalcaemia and/or hypokalaemia (see section 4.8). In most affected patients, hypomagnesaemia (and hypomagnesaemia associated hypocalcaemia and/or hypokalaemia) improved after magnesium replacement and discontinuation of the PPI.

For patients expected to be on prolonged treatment or who take PPIs with digoxin or medicines that may cause hypomagnesaemia (e.g. diuretics), health care professionals should consider measuring magnesium levels before starting PPI treatment and periodically during treatment.

***Bone fractures***

Proton pump inhibitors, especially if used in high doses and over long durations (> 1 year), may modestly increase the risk of hip, wrist and spine fracture, predominantly in the elderly or in the presence of other recognised risk factors. Observational studies suggest that proton pump inhibitors may increase the overall risk of fracture by 10-40 %. Some

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of this increase may be due to other risk factors. Patients at risk of osteoporosis should receive care according to current clinical guidelines and they should have an adequate intake of vitamin D and calcium.

**Severe Cutaneous Adverse Reactions (SCAR)**

Severe cutaneous adverse reactions, including erythema multiforme, Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), drug reaction with eosinophilia and systemic symptoms (DRESS), and acute generalized exanthematous pustulosis (AGEP) have been reported in association with the use of PPIs (see Undesirable Effects, 4.8). Discontinue pantoprazole at the first signs or symptoms of severe cutaneous adverse reactions or other signs of hypersensitivity and consider further evaluation.

***Subacute cutaneous lupus erythematosus (SCLE)***

Proton pump inhibitors are associated with very infrequent cases of SCLE. If lesions occur, especially in sun exposed areas of the skin, and if accompanied by arthralgia, the patient should seek medical help promptly and the healthcare professional should consider stopping **PANTOLOC®**. SCLE after previous treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.

***Interference with laboratory tests***

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

***PANTOLOC®*** *contains sodium*

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially ‘sodium-free’.

***Mannitol in excipients***

Patients with the rare hereditary condition of mannitol intolerance should not take **PANTOLOC®**.

**Hepatic impairment**

In patients with mild to moderate liver impairment, the liver enzymes should be monitored regularly during treatment with 40 mg **PANTOLOC®**, particularly on long-term use. In the case of a rise of the liver enzymes, the treatment should be discontinued (see section 4.2).

Use of **PANTOLOC® 20** as preventative of gastroduodenal ulcers, induced by non-selective non-steroidal anti-inflammatory drugs (NSAIDs) should be restricted to patients who require continued NSAID treatment and have an increased risk to

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develop gastrointestinal complications.

**PANTOLOC®** is not indicated for mild gastro-intestinal complaints such as nervous dyspepsia.

In the presence of any alarming symptoms (e.g., significant unintentional weight loss, recurrent vomiting, dysphagia, haematemesis or malaena) and when gastric ulcer is suspected or present, malignancy should be excluded, as treatment with **PANTOLOC®** may alleviate symptoms and delay diagnosis.

Daily treatment with any acid-blocking medicines including **PANTOLOC®** over a long period of time (e.g., longer than 3 years) may lead to malabsorption of cyanocobalamin caused by hypo- or achlorhydria. Cases of cyanocobalamin deficiency under acid-blocking therapy have been reported in the literature. This should be considered when respective clinical symptoms are observed.

**4.5 Interaction with other medicinal products and other forms of interaction**

***Concomitant intake of food has no influence on the bioavailability.***

The active ingredient of **PANTOLOC®** is metabolised in the liver via the cytochrome P450 enzyme system. An interaction of **PANTOLOC®** with other medicines or compounds which are metabolised using the same enzyme system cannot be excluded. No clinically significant interactions were, however, observed in specific tests with a number of such medicines or compounds, namely antipyrine, caffeine, carbamazepine, diazepam, diclofenac, digoxin, ethanol, glibenclamide, metoprolol, naproxen, nifedipine, phenprocoumon, phenytoin, piroxicam, theophylline, warfarin and oral contraceptives.

***Coumarin anticoagulants***

However, the response to anticoagulants such as warfarin, phenprocoumon and acenocoumarol may be affected by any concomitant medication. It is therefore good practice to monitor the patient with additional PT (prothrombin time) /INR (international normalised ratio) determinations when **PANTOLOC®** is initiated, discontinued or taken irregularly. Due to long lasting inhibition of gastric acid secretion **PANTOLOC®** may reduce the absorption of medicines with a gastric pH-dependent bioavailability, e.g. some azole antifungals like ketoconazole, itraconazole, posaconazole and other medicines like erlotinib.

***HIV Protease Inhibitors***

Co-administration of pantoprazole is contraindicated with HIV protease inhibitors for which absorption is dependent on acidic intragastric pH such as atazanavir, nelfinavir; due to significant reduction in their bioavailability (see Contraindications, 4.3).

There were no interactions with concomitantly administered antacids.

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***Methotrexate***

Concomitant use of PPIs, including **PANTOLOC®,** with methotrexate (primarily at high dose), may elevate and prolong serum levels of methotrexate and/or its metabolite hydroxymethotrexate, possibly leading to methotrexate toxicities.

***Effects of Other Medicines on Pantoprazole***

**Drugs that Inhibit or Induce CYP2C19**

Inhibitors of CYP2C19, such as fluvoxamine, would likely increase the systemic exposure to pantoprazole. Inducers of CYP2C19 may decrease the systemic exposure to pantoprazole.

### *4.6 Fertility, pregnancy and lactation*

Safety in pregnancy and during lactation has not been established.

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

**PANTOLOC®** may have an influence on the ability to drive and use machines and the individual patient's response must be assessed.

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## 4.8 Undesirable effects

Very common (≥1/10); common (≥1/100, < 1/10); uncommon (≥1/1000, < 1/100); rare (≥ 1/10 000, < 1/1000) very rare (≤ 1/10 000) including isolated cases, not known (cannot be estimated from the available data).

| **MEDRA System Organ Class** | **Frequency** | | | | |
|---|---|---|---|---|---|
| | **Common** | **Uncommon** | **Rare** | **Very rare** | **Not known** |
| Blood and lymphatic system disorders | | | Agranulocytosis | Thrombocytopenia; Leukopenia; Pancytopenia | |
| Immune system disorders | | | Hypersensitivity (including anaphylactic reactions and anaphylactic shock) | | |
| Metabolism and nutrition disorders | | | Hyperlipidaemias and lipid increases (triglycerides, cholesterol); Weight changes | | Hyponatraemia; Hypomagnesaemia (see section 4.4); Hypocalcaemia(1); Hypokalaemia(1) |
| Psychiatric disorders | | Sleep disorders | Depression (and all aggravations) | Disorientation (and all aggravations) | Hallucination; Confusion (especially in pre-disposed patients, as well as the aggravation of these symptoms in case of pre-existence) |
| Nervous system disorders | | Headache; Dizziness | Taste disorders | | Paraesthesia |
| Eye disorders | | | Disturbances in vision / blurred vision | | |
| Gastrointestinal disorders | Fundic gland polyps (benign) | Diarrhoea; Nausea / vomiting; Abdominal distension and bloating; Constipation; Dry mouth; Abdominal pain and discomfort | | | Microscopic colitis |
| Hepatobiliary disorders | | Liver enzymes increased (transaminases, γ-GT) | Bilirubin increased | | Hepatocellular injury; Jaundice; Hepatocellular failure |

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| | | | | | |
|---|---|---|---|---|---|
| Skin and subcutaneous tissue disorders | | Rash / exanthema / eruption; Pruritus | Urticaria; Angioedema | | Stevens-Johnson syndrome; Toxic epidermal Necrolysis; Lyell syndrome; Drug reaction with eosinophilia and systemic symptoms; Acute generalized exanthematous pustulosis; Erythema multiforme; Photosensitivity; Subacute cutaneous lupus erythematosus (see section 4.4); Drug reaction with eosinophilia and systemic symptoms (DRESS) |
| Musculoskeletal and connective tissue disorders | | Fracture of the hip, wrist or spine (see section 4.4) | Arthralgia; Myalgia | | Muscle spasm[(2)] |
| Renal and urinary disorders | | | | | Tubulointerstitial nephritis (TIN) (with possible progression that may lead to chronic renal failure) |
| Reproductive system and breast disorders | | | Gynaecomastia | | |
| General disorders and administration site conditions | Injection site thrombophlebitis† | Asthenia, fatigue and malaise | Body temperature increased; Oedema peripheral | | |

1. Hypocalcaemia and/or hypokalaemia may be related to the occurrence of hypomagnesaemia (see section 4.4).

2. Muscle spasm as a consequence of electrolyte disturbance.

† Applicable to pantoprazole 40 mg I.V. only

**Post-marketing reports:**

***Hepatobiliary disorders*:** Hepatocellular injury, jaundice, hepatocellular failure

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

***Renal and urinary disorders*:** Interstitial nephritis

***Skin and subcutaneous tissue disorders*:** Stevens-Johnson syndrome, Lyell syndrome (Toxic epidermal necrolysis),

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erythema multiforme, photosensitivity

***Infections and infestations*:** *Clostridium difficile*-associated diarrhoea.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are asked to report any suspected adverse reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website. Additionally, suspected adverse reactions can be reported to AE.SouthafricaSSA@takeda.com or on the 24 hours contact number: 082 525 3040.

### *4.9 Overdose*

There are no known symptoms of overdosage in man. No specific therapeutic recommendation can be made in cases of overdosage.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group:

A 11.4.3 Medicines acting on the gastro-intestinal tract.

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**Mechanism of Action**

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

Pantoprazole is a substituted benzimidazole which accumulates in the acidic compartment of the parietal cells after absorption. In the parietal cell it is protonated and chemically re-arranged to the active inhibitor, a cyclic sulphenamide, which binds to the $H^+$,$K^+$-ATPase, thus inhibiting the proton pump and causing suppression of stimulated and basal gastric acid secretion after single and multiple intravenous and oral pantoprazole dosing. Because pantoprazole acts distal to the receptor level, it can influence gastric acid secretion irrespective of the nature of the stimulus.

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

**Effect on gastric acid secretion**

Following oral or intravenous administration, pantoprazole inhibits the pentagastrin-stimulated gastric acid secretion. The mean acid inhibition was 85 %, 2½ to 3½ hours after dosing with pantoprazole 40 mg/day for 7 days. With 30 mg pantoprazole intravenous, the mean acid inhibition after 5 days was 99 %. Basal 24 hour acidity was reduced by 98 %.

After stopping the administration of pantoprazole, there is no evidence of rebound hypersecretion and 7 days after administering the last dose the acid output is normal.

Pantoprazole maintains the physiological pH rhythm. The values, however, are shifted to higher levels. During the night, periods with pH values approximating placebo have been found to occur.

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

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**5.2 Pharmacokinetic properties**

**Absorption and distribution**

**Oral:**

Pantoprazole is unstable in acid and is administered orally in the form of an enteric-coated tablet. Absorption takes place in the small intestine. On average, the maximum plasma concentrations are approximately 2 to 3 µg/ml about 2½ hours after administration of 40 mg pantoprazole daily, as a single or multiple dose in healthy volunteers. The absolute systemic bioavailability of pantoprazole from single and multiple oral doses of pantoprazole is approximately 77 %.

**Intravenous:**

Following intravenous administration of pantoprazole, plasma concentrations decline biexponentially. The terminal half-life ($t_{½}$) is about 1 hour. The total serum clearance is approximately 0,1 l/h/kg and the volume of distribution is about 0,15 l/kg, respectively.

The plasma kinetics for pantoprazole after both oral and intravenous administration are linear over the dose range 10-80 mg.

**Metabolism**

Pantoprazole is almost exclusively metabolised in the liver. The main metabolite is desmethylpantoprazole, which is conjugated with sulphate.

**Elimination**

Renal elimination represents the most important route of excretion (approximately 80 %) for the metabolites of pantoprazole. The balance is excreted with the faeces. The half-life of the main metabolite is approximately 1½ hours which is slightly longer than that of pantoprazole.

**Pharmacokinetic profile in patients with impaired liver or renal function**

For patients with mild to moderately severe hepatic cirrhosis the elimination half-life values increase to between 7 to 9 hours. The AUC values increase by a factor of 5 to 8, while the maximum serum concentration only increases by a factor of 1,5 in comparison with healthy subjects. In patients with renal impairment the half-life of the main metabolite is moderately increased but there is no accumulation at therapeutic doses. The half-life of pantoprazole in patients with renal impairment is comparable to the half-life of pantoprazole in healthy subjects. Pantoprazole is poorly dialysed. A slight

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increase in AUC and $C_{max}$ occurs in elderly volunteers compared with younger people.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

**PANTOLOC® 20**

Excipients include: sodium carbonate, mannitol, crospovidone, polyvidone K90, calcium stearate, hypromellose 2910, polyvidone K25, titanium dioxide, yellow ferric oxide, propylene glycol, methacrylic acid-ethyl and triethyl citrate.

**PANTOLOC® 40**

Excipients include: sodium carbonate, mannitol, crospovidone, polyvidone K90, calcium stearate, hypromellose 2910, polyvidone K25, titanium dioxide, yellow ferric oxide, propylene glycol, methacrylic acid-ethyl and triethyl citrate.

**PANTOLOC® IV**

Excipients include: edentate disodium dehydrate, sodium hydroxide

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### 6.2 Incompatibilities

In the absence of compatibility studies, this medicine must not be mixed with other medicines except those mentioned in **Section 6.6**.

### 6.3 Shelf life

**PANTOLOC® 20 and 40**: 3 years.

**PANTOLOC® IV**: 2 years.

### 6.4 Special precautions for storage

**PANTOLOC® 20 and 40 Tablets**: Store at or below 30 °C.

**PANTOLOC® IV**: Store at or below 25 °C.

Protect from light.

**KEEP OUT OF REACH OF CHILDREN.**

### 6.5 Nature and contents of container

**PANTOLOC®** 20 blister packs of 28 tablets

**PANTOLOC®** 40 blister packs of 14 or 28 tablets

**PANTOLOC®** IV vial with lyophylised powder (1 x 5 vials)

### 6.6 Special precautions for disposal and other handling

**General precautions**

Procedures for proper handling and disposal of medicines should be considered.

***Disposal***

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

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## 7. HOLDER OF CERTIFICATE OF REGISTRATION

**TAKEDA (Pty) Ltd**

Building A,

Monte Circle

64 Montecasino Boulevard

Fourways

2191

South Africa

## 8. REGISTRATION NUMBER(S)

**PANTOLOC® 20:** 34/11.4.3/0005

**PANTOLOC® 40:** 28/11.4.3/0407

**PANTOLOC® IV:** 33/11.4.3/0041

**Namibia:**
**PANTOLOC® 20:** 05/11.4.3/0395
**PANTOLOC® 40:** 05/11.4.3/0396
**PANTOLOC® IV:** 05/11.4.3/0397

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

25 April 2013

## 10. DATE OF REVISION OF THE TEXT

18 February 2026