NEW ZEALAND DATA SHEET

1 PRODUCT NAME

Pantoprazole-AFT 40 mg powder for injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each vial contains 40 mg of pantoprazole (as pantoprazole sodium sesquihydrate). Following reconstitution and mixing, the concentration of pantoprazole in solution is 0.8 mg/mL.

For the full list of excipients, see Section 6.1 List of excipients.

3 PHARMACEUTICAL FORM

Pantoprazole - AFT is a white to off-white powder for solution for injection.

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Pantoprazole – AFT is indicated for short-term use where oral therapy is not appropriate for:

1. Symptomatic improvement and healing of gastrointestinal diseases which require a reduction in acid secretion:
    - Duodenal ulcer
    - Gastric ulcer
    - Reflux oesophagitis
    - Gastrointestinal lesions refractory to H2 blockers
    - Zollinger-Ellison Syndrome
2. Maintenance of healed reflux oesophagitis in patients previously treated for moderate to severe reflux oesophagitis.

Note: Patients whose gastric or duodenal ulceration is not associated with ingestion of non-steroidal anti-inflammatory drugs require treatment with anti-microbial agents in addition to anti-secretory drugs, whether on first presentation or recurrence.

4.2 DOSE AND METHOD OF ADMINISTRATION

Dosage

Duodenal ulcer, gastric ulcer, gastrointestinal lesions refractory to H2 blockers, Zollinger-Ellison syndrome	40 mg per day
Reflux oesophagitis	20–40 mg per day

Intravenous Pantoprazole-AFT should be replaced with oral therapy as soon as practicable.

Method of administration

For instructions on reconstitution and dilution of the medicine before administration, see Section 6.6.

After preparation, the solution should be administered over 2 to 15 minutes.

Use in special population

Infants and children

There are no data currently available on the use of pantoprazole in children.

Use in elderly

The usual daily dose of 20 mg or 40 mg can be given.

Use in patients with renal impairment

The usual daily dose of 20 mg or 40 mg can be given.

Use in patients with hepatic impairment

Pantoprazole is contraindicated in patients with cirrhosis or severe liver disease (see Section 4.3 CONTRAINDICATIONS). With milder forms of liver disease, the initial dose should be reduced.

4.3 CONTRAINDICATIONS

Known hypersensitivity to pantoprazole, substituted benzimidazoles or any other components of the formulation or in cases of cirrhosis or severe liver disease.

Pantoprazole, like other proton pump inhibitors, should not be co-administered with HIV protease inhibitors, such as atazanavir or nelfinavir (see Section 4.5 INTERACTIONS WITH OTHER MEDICINES).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Check the following before use

The intravenous administration of Pantoprazole-AFT powder for injection is recommended only if oral application is not appropriate.

In the presence of any alarm symptoms (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.

Clostiridum difficile

PPI therapy may be associated with an increased risk of Clostridium difficile infection. 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*, *Campylobacter* and *C. difficile*.

Bone fractures

PPI therapy may be associated with an increased risk for osteoporosis-related fractures of the hip, wrist, or spine. The risk of fracture was increased in patients who received high-doses; defined as multiple daily doses, and long-term PPI therapy (a year or longer).

Acute Interstitial Nephritis

Acute interstitial nephritis has been observed in patients taking PPIs including pantoprazole. Acute interstitial nephritis may occur at any point during PPI therapy and is generally associated to an idiopathic hypersensitivity reaction. Discontinue pantoprazole if acute interstitial nephritis develops.

Hypomagnesaemia

Hypomagnesaemia has been rarely reported in patients treated with PPIs for at least three months (in most cases after a year of therapy). Serious consequences of hypomagnesaemia include tetany, arrhythmia, and seizure.

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.

Use in the elderly

The usual daily dose of 20 mg or 40 mg can be given.

Paediatric use

To date there has been no experience with treatment in children.

Effects on laboratory tests

Increased Chromogranin A (CgA) level may interfere with investigations for neuroendocrine tumours. To avoid this interference, proton pump inhibitor treatment should be stopped 14 days before CgA measurements.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

Pantoprazole is metabolised in the liver via the cytochrome P450 enzyme system. A study using human liver microsomes suggested that the P450 enzymes CYP2C19 and CYP3A4 are involved in its metabolism. In addition, CYP2D6 and CYP2C9-10 were implicated in another study. An interaction of pantoprazole with other drugs or compounds which are metabolised using the same enzyme system cannot be excluded. However, no clinically significant interactions were observed in specific tests with a number of such drugs or compounds, namely carbamazepine, caffeine, diazepam, diclofenac, digoxin, ethanol, glibenclamide, metoprolol, naproxen, nifedipine, phenytoin, piroxicam, theophylline, and the low dose oral contraceptive Triphasil (levonorgestrel and ethinyl oestradiol). There

was also no interaction with a concomitantly administered antacid (aluminium hydroxide and magnesium hydroxide).

Treatment of dogs with IV famotidine shortened the duration of the pH elevation effect of pantoprazole.

Four cross-over pharmacokinetic studies designed to examine any interactions between pantoprazole and the drugs clarithromycin, amoxicillin and metronidazole, conducted in 66 healthy volunteers, showed no interactions.

Drugs with pH-Dependent Absorption Pharmacokinetics

As with all acid suppressant medications, the absorption of drugs whose bioavailability is pH dependent (e.g. ketoconazole, itraconazole, posaconazole, erlotinib), might be altered due to the decrease in gastric acidity.

HIV Protease Inhibitors

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, proton pump inhibitors, including pantoprazole, should not be co-administered with HIV protease inhibitors for which absorption is dependent on acidic intragastric pH, such as atazanavir or nelfinavir. (see Section 4.3 – CONTRAINDICATIONS)

Mycophenolate mofetil

Co-administration of PPIs in healthy subjects and in transplant patients receiving mycophenolate mofetil has been reported to reduce the exposure to the active metabolite, mycophenolic acid. This is possibly due to a decrease in mycophenolate mofetil solubility at an increased gastric pH. The clinical relevance of reduced mycophenolic acid exposure on organ rejection has not been established in transplant patients receiving PPIs and mycophenolate mofetil. Use pantoprazole with caution in transplant patients receiving mycophenolate mofetil.

Methotrexate

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

Drugs that Inhibit or Induce CYP2C19 (tacrolimus, fluvoxamine)

Concomitant administration of pantoprazole and tacrolimus may increase whole blood levels of tacrolimus, especially in transplant patients who are intermediate or poor metabolisers of CYP2C19. Inhibitors of CYP2C19, such as fluvoxamine, would likely increase the systemic exposure of pantoprazole.

Coumarin anticoagulants (phenprocoumon or warfarin)

Co-administration of pantoprazole with warfarin or phenprocoumon did not affect the pharmacokinetics of warfarin, phenprocoumon or international normalised ratio (INR). However, there have been reports of increased INR and prothrombin time in patients receiving PPIs and warfarin or phenprocoumon concomitantly. Increases in INR and prothrombin time may lead to abnormal bleeding, and even death. Therefore, in patients being treated with coumarin anticoagulants (e.g. warfarin or phenprocoumon), monitoring of prothrombin time / INR is recommended after initiation, termination or during irregular use of pantoprazole.

4.6 FERTILITY, PREGNANCY AND LACTATION

Use in pregnancy

Category B3

Teratological studies in rats and rabbits gave no evidence of a teratogenic potential for pantoprazole. In oral rat studies, dose-dependent toxic effects were observed on fetuses and pups: increased pre- and postnatal deaths at 450 mg/kg/day, reduced fetal weight at ≥150 mg/kg/day and delayed skeletal ossification and reduced pup growth at ≥15 mg/kg/day. For the latter a no-effect dose was not established. Doses of 450 mg/kg/day were maternotoxic and may have been associated with dystocia and incomplete parturition. Penetration of the placenta was investigated in the rat and was found to increase with advanced gestation. As a result, concentrations of pantoprazole in the fetus are increased shortly before birth regardless of the route of administration.

The significance of these findings in humans is unknown. As there is no information on the safety of the drug during pregnancy in women, pantoprazole should not be used during pregnancy, unless the benefit clearly outweighs the potential risk to the fetus.

Use in lactation

A peri/post-natal study in rats found that treatment with pantoprazole at doses of 10 mg/kg/day or greater decreased pup growth. A transient effect on one of a series of development tests (startle response) was only evident in the 30 mg/kg/day group at an age when male and female offspring showed lower body weights, paralleled with lower brain weight, than the controls. The significance of these findings for humans is unknown, and there is currently no information on the safety of pantoprazole during breast feeding in humans. Excretion into human milk has been reported. Therefore, pantoprazole should only be used during lactation if the benefits clearly outweigh the risks.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

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

4.8 ADVERSE EFFECTS (UNDESIREABLE EFFECTS)

Pantoprazole injection is well tolerated. Most of the adverse reactions seen with treatment were of mild or moderate intensity. The following adverse reactions have been

reported in patients receiving pantoprazole alone or in combination with antibiotics for H. pylori eradication in clinical trials and postmarketing surveillance.

Adverse reactions within each body system are listed in descending order of frequency (Very common: ≥10%; common: ≥1% and <10%; uncommon: ≥0.1% and <1%; rare ≥0.01% and <0.1%; very rare: <0.01%; not known: cannot be estimated from the available data). These include the following:

General disorders and administration site conditions

Common: Injection site thrombophlebitis

Uncommon: Fatigue and malaise, asthenia and increased sweating

Rare: fever, peripheral oedema

Very rare: substernal chest pain and hot flushes

Cardiovascular disorders general

Rare: hypertension

Very rare: circulatory collapse

Nervous system disorders

Uncommon: headache, dizziness

Rare: taste disorders, metallic taste

Very rare: reduced movement and speech disorder, changes to the senses of smell and taste

Gastrointestinal system disorders

Uncommon: diarrhoea, nausea/vomiting, abdominal distension and bloating, constipation, dry mouth, abdominal pain and discomfort

Rare: rectal disorder and colonic polyp

Very rare: faecal discolouration and increased saliva

Not known: severe eructation

Hearing and vestibular disorders

Very rare: tinnitus

Immune system disorders

Rare: hypersensitivity (including anaphylactic reactions and anaphylactic shock)

Hepatobiliary disorders

Uncommon: liver enzymes increased

Rare: bilirubin increased

Very rare: hepatocellular failure, cholestatic hepatitis and jaundice

Not known: hepatocellular injury

The occurrence of severe hepatocellular damage leading to jaundice or hepatic failure having a temporal relationship to the oral administration of pantoprazole has been reported with a frequency of approximately one in a million patients.

Metabolism and nutrition disorders

Rare: hyperlipidaemias and lipid increases (triglycerides, cholesterol), weight changes
Not known: hyponatraemia, hypomagnesaemia

Musculoskeletal and connective tissue disorders

Rare: myalgia and arthralgia

Very rare: pain including skeletal pain

Not known: fracture of wrist, hip and spine

Renal and urinary disorders

Very rare: interstitial nephritis

Platelet, bleeding, clotting disorders

Very rare: increased coagulation time

Psychiatric disorders

Uncommon: sleep disorders

Rare: depression, hallucination, disorientation and confusion, especially in pre-disposed patients, as well as the aggravation of these symptoms in case of pre-existence.

Very rare: anxiety

Blood and lymphatic system disorders

Rare: anaemia, agranulocytosis

Very rare: leukopenia, thrombocytopenia, pancytopenia

Resistance mechanism disorders

Rare: sepsis

Respiratory system disorders

Very rare: dyspnoea

Reproductive system and breast disorders

Rare: gynaecomastia

Skin and subcutaneous tissue disorders

Uncommon: pruritus, rash/ exanthema/ eruption

Rare: angioedema and urticaria

Very rare: flushing, severe skin reactions such as Stevens Johnson Syndrome, toxic epidermal necrolysis, erythema multiforme, Lyell Syndrome; and photosensitivity

Not known: subacute cutaneous lupus erythematosus

Eye disorders

Uncommon: disturbances in vision (blurred vision)

Very rare: conjunctivitis

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration of the medicinal product is important. It allows continued monitoring of the benefit-risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions at https://nzphvc.otago.ac.nz/reporting.

4.9 OVERDOSE

There are no known symptoms of overdosage in humans. In individual cases, 240 mg was administered i.v. or p.o. and was well tolerated. Standard detoxification procedures apply.

For information of the management of overdose, contact the National Poisons Centre on 0800 Poison (0800 764 766).

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

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

The substance is a substituted benzimidazole which accumulates in the acidic environment of the parietal cells after absorption. There, it is converted into the active form, a cyclic sulfenamide which binds to the H+/K+-ATPase, thus inhibiting the proton pump and causing potent and long-lasting suppression of basal and stimulated gastric acid secretion. As pantoprazole acts distal to the receptor level, it can influence gastric acid secretion irrespective of the nature of the stimulus (acetylcholine, histamine, gastrin).

Oral and intravenous pantoprazole 40 mg/day for 5 days had equivalent effect on intra-gastric pH in 20 healthy adult male volunteers in a randomised, open, 2-period crossover trial with 14-day wash-out. The pre-defined equivalence range was ±20% for percentage

of time with pH<3 and 4 and ±1 pH unit for 24 h median pH. The 24 h median pH on day 5 was 2.7 on oral treatment and 3.2 on intravenous treatment.

Pantoprazole's selectivity is due to the fact that it only exerts its full effect in a strongly acidic environment (pH<3), remaining mostly inactive at higher pH values. As a result, its complete pharmacological, and thus therapeutic effect, can only be achieved in the acid-secretory parietal cells. By means of a feedback mechanism this effect is diminished at the same rate as acid secretion is inhibited.

As with other proton pump inhibitors and H2 receptor inhibitors, treatment with pantoprazole causes a reduced acidity in the stomach and thereby an increase in gastrin in proportion to the reduction in acidity. The increase in gastrin is reversible.

Clinical trials

Two uncontrolled trials in adults assessed the efficacy of pantoprazole 40 mg/day, administered intravenously for 5-7 days then orally for 3-7 weeks, in the endoscopic healing of Savary-Miller stage 2-3 reflux oesophagitis (Table 1). Using historical data, it was concluded that the intravenous plus oral regimen was at least equivalent to an exclusively oral regimen. The criterion for at least equivalence was: lower limit of 90% confidence interval of the difference, (IV + oral) - oral, > -15%.

Table 1: Pantoprazole 40 mg/day (IV plus oral) in endoscopic healing of Stage 2-3 oesophagitis (Intention to treat[1])

Trial	N	% patients healed	
		4 weeks	8 weeks
FK3050	176	65	75
BAT010	110	77	85
Historical (oral)[2]	357	64	77

[1]Protocol violators counted as non-responders

[2]Trials FK3005, FK3009

5.2 PHARMACOKINETIC PROPERTIES

A considerably higher C_{max} occurs after intravenous administration compared with oral administration. In a study in healthy volunteers given 40 mg/day for 5 days, the steady state C_{max} was 5.9 mg/L after intravenous administration and 1.7 mg/L after oral administration. Terminal half-life is approximately 1 hour. Pharmacokinetics do not vary after single or repeated administration. The plasma kinetics of pantoprazole are linear (in the dose range of 10 to 80 mg) after both oral and intravenous administration. The serum protein binding of pantoprazole is approximately 98%.

Distribution

Volume of distribution is approximately 0.15 L/kg and clearance is approximately 0.1 L/h/kg.

Excretion

Pantoprazole is rapidly eliminated from serum and is almost exclusively metabolised in the liver. Renal elimination represents the most important route of excretion (approximately 80%) for the metabolites of pantoprazole, the rest are excreted with the faeces. The main metabolite in both the serum and urine is desmethyl-pantoprazole which is conjugated with the sulfate. The half-life of the main metabolites (approximately 1.5 h) is not much longer than that of pantoprazole.

In studies in healthy volunteers, 2% of subjects showed a slower elimination of pantoprazole from serum/plasma, with an increase in terminal elimination half-life of up to 10 hours.

Patients with a half-life of greater than 3.5 hours and with an apparent clearance of less than 2 L/h/kg are considered to be slow metabolisers of pantoprazole.

In patients with liver impairment, pantoprazole elimination is significantly delayed. After a 40 mg tablet, AUC increased by a factor of 6-8 and terminal half-life increased from 1 hour to 7-9 hours in patients with liver cirrhosis compared with healthy subjects. In patients with renal impairment (including those undergoing dialysis), no dose reduction is required. Although the main metabolite is moderately increased, there is no accumulation.

The half-life of pantoprazole is as short as in healthy subjects. Pantoprazole is poorly dialyzable.

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

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

A number of in vitro and in vivo genotoxicity assays covering mutagenicity, clastogenicity and DNA damage end points were conducted on pantoprazole and the results were generally negative. Exposures achieved in the in vivo tests in mice and rats were well in excess of exposures expected clinically. However, pantoprazole was clearly positive in carefully conducted cytogenetic assays in human lymphocytes in vitro, both in the presence and absence of metabolic activation. Omeprazole was also positive in a comparable test conducted in the same laboratory, suggesting a possible class effect. A minute amount of radioactivity was bound to rat hepatic DNA after treatment with 200 mg/kg/day pantoprazole for 14 days. However, no distinct DNA- adduct has been detected.

Carcinogenicity

A two-year oral carcinogenicity study in Sprague Dawley rats at doses up to 200 mg/kg/day showed gastric carcinoids after pantoprazole treatment at doses greater than 0.5 mg/kg/day in females and greater than 5 mg/kg/day in males, with none observed in controls. The development of gastric tumours is attributed to chronic

elevation of serum gastrin levels with associated histopathological changes in the gastrointestinal system.

In both male and female rats, the development of hepatocellular adenomas was increased at doses greater than 5 mg/kg/day and the development of hepatocellular carcinomas was increased at doses greater than 50 mg/kg/day. Hepatocellular tumours, which were also observed in female mice at oral doses greater than 25 mg/kg/day, may be associated with pantoprazole-induced increases in hepatic enzyme activity.

Treatment with pantoprazole at doses greater than 50 mg/kg/day also increased the development of thyroid follicular cell adenomas in male and female rats. Several studies in rats were conducted to investigate the effect of pantoprazole on the thyroid, the results of which suggested that the effect may be secondary to the induction of enzymes in the liver.

In a more recent carcinogenicity study, Fischer rats were studied using lower doses (5, 15 and 50 mg/kg). Gastric carcinoids were detected at all doses in females and at the 15 and 50 mg/kg doses in males and none were detected in controls. No metastases of these carcinoids were detected. There was no increase in incidence of liver tumours. The dose of 15 mg/kg is seen to be the no-effect level for liver tumours in rodents.

Consideration of the possible mechanisms involved in the development of the above medicine-related tumour types suggests that it is unlikely that there is any carcinogenic risk in humans at therapeutic dose levels of pantoprazole for short term treatment.

Mutagenesis

Pantoprazole was found to be negative in the following studies: *in vivo* chromosome aberration assay in rat and bone marrow (126E/95), mouse lymphoma test (222E/95) and a gene mutation test in Chinese hamster ovary cells (*in vitro*) (188E/95). In addition, toxicokinetic studies were conducted in rats at the doses used in the bone marrow assay (50 to 1200 mg/kg) (56E/96) and in mice at the high dose from the earlier micronucleus test (710 mg/kg) (89E/96). In both species, pantoprazole exposure was high with the AUCs being 26 to 30 times higher in the rat or mouse respectively, than humans using the 20 mg tablet.

General toxicity

Gastrointestinal system

Treatment with pantoprazole causes dose-dependent hypergastrinaemia as a result of inhibition of gastric acid secretion. Gastrin has a trophic effect on the gastricmucosa, and increases in gastric weight have been observed in rats and dogs to be dependent upon both dose and duration of treatment. Accompanying histopathological changes in the gastric mucosa were increased height, dilatation of fundic glands, chief cell hyperplasia and/or atrophy and parietal cell hyperplasia or vacuolation/degeneration. Increased density of enterochromaffin-like (ECL) cells was observed after 12 months treatment at dose levels from 5 mg/kg/day in rats and 2.5 mg/kg/day in dogs; all changes were reversible after various recovery periods. Since these gastric effects are a consequence of

the pharmacological effect of acid secretion inhibition, no-effect doses were not established in all instances.

Although rats might be more susceptible to this effect than other species because of their high ECL cell density and sensitivity to gastrin, ECL cell hyperplasia occurs in other species, including mice and dogs, and has been observed in one of two clinical trials in which ECL cell density was measured (a 2-fold increase was observed in study RR126/97 after up to 5 years of treatment with regular and high doses, but no increase was observed in study RR125/97). No dysplasic or neoplastic changes were observed in gastric endocrine cells in either study.

Ocular toxicity and dermal phototoxicity/ sensitivity

Studies have shown that pantoprazole is retained in low levels in the eyes and skin of pigmented rats. It is likely that the retention reflects a reversible association with melanin. Animal studies investigating the potential for phototoxicity/photosensitivity have not been conducted. A 2-week dog study, conducted specifically to investigate the effects on the eye and ear, did not reveal any changes relating to pantoprazole treatment, but the doses chosen were relatively low (40 and 160 mg (about 4 and 15 mg/kg) orally and 60 mg (about 6 mg/kg) IV). No ophthalmological changes or changes in electroretinographs were observed in cynomolgus monkeys at IV doses of up to 15 mg/kg/day for 4 weeks.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Mannitol

Tribasic sodium phosphate dodecahydrate

6.2 INCOMPATIBILITIES

This medicinal product must not be mixed with other medicinal products except those mentioned in Section 4.2 Dose and method of administration.

6.3 SHELF LIFE

36 months

The reconstituted solution should be used within 6 hours and the diluted solution should be used within 12 hours when stored below 25 °C. However, to reduce microbiological hazard, use as soon as practicable after reconstitution/preparation.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Store below 25 °C. Keep the vial in the outer carton to protect from light.

For storage conditions after reconstitution and dilution of the medicine, see Section 6.3.

6.5 NATURE AND CONTENTS OF CONTAINER

Pantoprazole-AFT 40 mg powder for injection contains 40 mg pantoprazole (as sodium sesquihydrate), a white to off white powder, in a clear glass vial with a blue rubber stopper and aluminium "flip-off" cap. 10 vials are packed in a carton.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL AND OTHER HANDLING

A ready-to-use solution is prepared by injecting 10 mL Sodium Chloride Intravenous Infusion 0.9% into the vial containing the dry powder. This reconstituted solution may be administered directly or may be administered after mixing with 0.9% Sodium Chloride Intravenous Infusion or 5% Glucose Intravenous Infusion or Ringer's Lactate injection. For reconstitution and mixing, follow the below mentioned procedure:

Dissolve a vial of pantoprazole lyophilisate for solution for injection with 10 ml of 0.9% sodium chloride injection. Transfer 2 vials of reconstitution solution of pantoprazole lyophilisate for solution for injection to 80 ml of 0.9% sodium chloride injection, 5% glucose injection or Ringer's lactate injection respectively, to obtain the diluted solution of a total volume of 100 ml and the concentration of 0.8 mg/ml.

This product contains no antimicrobial agent. Pantoprazole-AFT injection is for single use in one patient only. Any unused product remaining or the visual appearance of which has changed (e.g., if cloudiness or precipitation is observed), should be discarded.

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

7 MEDICINE SCHEDULE (POISONS STANDARD)

S4 – Prescription only medicine

8 SPONSOR

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9 DATE OF FIRST APPROVAL

4 August 2022