Pantoprazole Auxilto Powder For Solution For Injection 40mg

1. Name of the medicinal product

Pantoprazole Auxilto Powder For Solution For Injection 40mg

2. Composition

Each vial contains

Active ingredient(s):

Pantoprazole (as pantoprazole sodium sesquihydrate) 40mg

Excipient(s):

Disodium edetate, Mannitol, Sodium hydroxide.

3. Pharmaceutical form

Dosage form:

Powder for solution for injection (lyophilized powder).

Product description:

White or almost white lyophilized powder, contained in glass vial, sealed with a grey rubber stopper and an aluminium flip-off cap.

Description after reconstitution:

The solution after reconstitution is clear and colorless.

4. Indications

Short-term use for symptomatic improvement and healing of gastrointestinal diseases which require a reduction in acid secretion:

- Duodenal ulcer
- Gastric ulcer
- Moderate and severe reflux esophagitis
- Zollinger-Ellison-Syndrome and other pathological hypersecretory conditions

5. Dosage and administration

The intravenous administration of Pantoprazole I.V. is recommended only if oral application is not appropriate. The recommended dose for gastric and duodenal ulcer and moderate and severe reflux esophagitis is one vial of 40mg Pantoprazole I.V. per day. For the long-term management of Zollinger-Ellison-Syndrome and other pathological hypersecretory conditions the recommended daily dose at the beginning of the treatment is 80mg Pantoprazole I.V. Thereafter, the dosage can be titrated up or down as needed using measurements of gastric acid secretion to guide. With doses above 80mg daily, the dose should be divided and given twice daily. A temporary increase of the dosage above 160mg 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 80mg 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. Transition from Pantoprazole I.V. to the oral formulation of pantoprazole should be performed as soon as it is clinically justified.

Special patient populations

Impaired hepatic function

A daily dose of 20mg pantoprazole (half a vial of 40mg Pantoprazole I.V.) should not be exceeded in patients with severe liver impairment.

Impaired renal function
No dose adjustment is necessary in patients with impaired renal function.

Type and duration treatment:
As soon as oral therapy is possible, treatment with Pantoprazole I.V. should be discontinued and 40mg pantoprazole p.o. should be administered instead.

Instruction for use/handling:
A ready-to-use solution is prepared by injecting 10ml of physiological sodium chloride solution into the vial containing the dry substance. This solution may be administered directly or may be administered after mixing it with 100ml physiological sodium chloride solution or 5% glucose.
Pantoprazole I.V. 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 not more than 25°C.
The drug should be administered intravenously over 2 – 15 minutes.

6. Contraindications
Pantoprazole I.V. should not be used in cases of known hypersensitivity to its constituents.

7. Special warnings and precautions for use

Bone fractures
Proton pump inhibitors (PPIs), especially if used in high doses and over long durations (> 1 year), may modestly increase the risk for osteoporosis-related fractures of the hip, wrist, or spine, predominantly in the elderly or in presence of other recognised risk factors.
Observational studies suggest that PPI may increase the overall risk of fracture by 10-40%. Some of this increase may be due to other risk factors. Patients at risk of osteoporosis should receive care according to current clinical guidelines and they should have an adequate intake of vitamin D and calcium.

Clostridium difficile
Published observational studies suggest that PPI therapy may be associated with an increased risk of *Clostridium difficile* associated diarrhea, especially in hospitalized patients. This diagnosis should be considered for diarrhea that does not improve. Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated.

Hypomagnesaemia
Severe hypomagnesaemia has been rarely reported in patients treated with PPI like pantoprazole for at least three months, and in most cases for a year. Serious manifestations of hypomagnesemia such as fatigue, tetany, delirium, dizziness, convulsions and ventricular arrhythmia can occur, but they may begin insidiously and be overlooked. In most affected patients, hypomagnesaemia improved after magnesium replacement and

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

Vitamin B12 Deficiency
In patients with Zollinger-Ellison syndrome and other pathological hypersecretory conditions requiring daily treatment with any acid-suppressing medications over a long period of time (e.g., longer than 3 years) may lead to malabsorption of cyanocobalamin (vitamin B12) caused by hypo- or achlorhydria. Rare reports of cyanocobalamin deficiency occurring with acid-suppressing therapy have been reported in the literature. This diagnosis should be considered if clinical symptoms consistent with cyanocobalamin deficiency are observed.

Interference with laboratory tests
Increased Chromogranin A (CgA) level may interfere with investigations for neuroendocrine tumours. If the patients are due to have a test on Chromogranin A level, pantoprazole treatment should be stopped for at least 5 days before CgA measurements to avoid this interference. 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.

Severe Cutaneous Adverse Reactions (SCARs)
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. Discontinue pantoprazole at the first signs or symptoms of severe cutaneous adverse reactions or other signs of hypersensitivity and consider further evaluation.

Hepatic impairment
In patients with severe liver impairment the liver enzymes should be monitored regularly during treatment with pantoprazole, particularly on long-term use. In the case of a rise of the liver enzymes, the treatment should be discontinued.

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, nelfinavir; due to significant reduction in their bioavailability.

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

Gastric malignancy

Symptomatic response to pantoprazole does not preclude the presence of gastric malignancy.

Regular surveillance

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

Sub-acute cutaneous lupus erythematosus (SCLE)

Proton pump inhibitors are associated with very infrequent cases of subacute cutaneous lupus erythematosus (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 the product. SCLE after previous treatment with a proton pump inhibitor may increase the risk of SCLE with other proton pump inhibitors.

8. Drug interactions

Drugs with pH Dependent Absorption Pharmacokinetics

Pantoprazole may interfere with the absorption of drugs where gastric pH is an important determinant of oral bioavailability.

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, nelfinavir; due to significant reduction in their bioavailability.

Methotrexate

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

Other Interaction Studies

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

An interaction of pantoprazole with other drugs or compounds, which are metabolized using the same enzyme system, cannot be excluded.

Results from a range of interaction studies demonstrate that pantoprazole does not affect 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 by administering pantoprazole concomitantly with the respective antibiotics (clarithromycin, metronidazole, amoxicillin). No clinically

relevant interactions were found.

Clopidogrel
Concomitant administration of pantoprazole and clopidogrel in healthy subjects had no clinically important effect on exposure to the active metabolite of clopidogrel or clopidogrel-induced platelet inhibition. No dose adjustment of clopidogrel is necessary when administered with an approved dose of pantoprazole.

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 metabolizers of CYP2C19. Inhibitors of CYP2C19, such as fluvoxamine, would likely increase the systemic exposure of pantoprazole.

Coumarin Anticoagulant (phenoprocoumon or warfarin)
Co-administration of pantoprazole with warfarin or phenoprocoumon did not affect the pharmacokinetics of warfarin, phenoprocoumon or INR. However, there have been reports of increased INR and prothrombin time in patients receiving PPIs and warfarin or phenoprocoumon concomitantly. Increases in INR and prothrombin time may lead to abnormal bleeding, and even death. Patients treated with pantoprazole and warfarin or phenoprocoumon may need to be monitored for increase in INR and prothrombin time.

9. Pregnancy and lactation

Pregnancy
A moderate amount of data on pregnant women (between 300-1000 pregnancy outcomes) indicates no malformative or feto/ neonatal toxicity of pantoprazole. Studies in animals have shown reproductive toxicity. The potential risk for humans is unknown. Pantoprazole should not be used during pregnancy unless clearly necessary.

Breastfeeding
Animal studies have shown excretion of pantoprazole in breast milk. There is insufficient information on the excretion into human milk but excretion into human milk has been reported. A risk to the newborn/infant cannot be excluded. 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 woman.

Fertility
There was no evidence of impaired fertility.

10. Effects on ability to drive and use machines

Pantoprazole has no or negligible influence on the ability to drive and use machines.
Adverse drug reactions, such as dizziness and visual disturbances may occur. If affected, patients should not drive or operate machines.

11. Adverse reactions

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.

Table 1: Adverse reactions with pantoprazole in clinical trials and post-marketing experience

System Organ Class (SOC)	Frequency	Undesirable effect
Blood and lymphatic system disorders	Rare	Agranulocytosis
	Very rare	Thrombocytopenia, leukopenia, pancytopenia
Eye disorders	Rare	Disturbances in vision/blurred vision
Gastrointestinal disorders	Common	Fundic gland polyps (benign)
	Uncommon	Diarrhoea, nausea/vomiting, abdominal distension and bloating, constipation, dry mouth, abdominal pain and discomfort
	Not known	Microscopic colitis
General disorders and administration site conditions	Common	Injection site thrombophlebitis
	Uncommon	Asthenia, fatigue and malaise
	Rare	Body temperature increased, oedema peripheral
Hepatobiliary disorders	Uncommon	Liver enzymes increased
	Rare	Bilirubin increased
	Not known	Hepatocellular injury, jaundice, hepatocellular failure
Immune system disorders	Rare	Hypersensitivity (including anaphylactic reactions and anaphylactic shock)
Infections and infestation	Not known	*Clostridium difficile* associated diarhhea
Metabolism and nutrition disorders	Rare	Hyperlipidaemias, weight changes
	Not known	Hyponatraemia, hypomagnesamia, vitamin B12 deficiency, Hypocalcaemia*, Hypokalaemia*.
Musculoskeletal and connective tissue disorders	Uncommon	Fracture of the hip, wrist or spine
	Rare	Arthralgia, myalgia
Nervous system disorders	Uncommon	Headache, dizziness
	Rare	Taste disorders
Psychiatric disorders	Uncommon	Sleep disorders
	Rare	Depression
	Very rare	Disorientation
	Not known	Hallucination, confusion
Renal and urinary disorders	Not known	Tubulointerstitial nephritis (TIN) (with possible progression to renal failure)

Reproductive system and breast disorders	Rare	Gynaecomastia
Skin and subcutaneous tissues disorders	Uncommon	Rash/exanthema/eruption, pruritus
	Rare	Urticaria, angioedema
	Not known	Stevens-Johnson syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms, acute generalized exanthematous pustulosis, erythema multiforme, photosensitivity, subacute cutaneous lupus erythematosus

*Hypocalcemia and/or hypokalaemia may be related to the occurrence of hypomagnesemia

12. Symptoms and treatment of overdose

There are no known symptoms of overdose in man. Systemic exposures with up to 240mg administered intravenously over 2 minutes were well tolerated. As pantoprazole is extensively protein bound, it is not readily dialysable. In case of overdose with clinical signs of intoxication, apart from symptomatic and supportive treatment, no specific therapeutic recommendations can be made.

13. Pharmacological properties

Pharmacotherapeutic group: Selective proton pump inhibitor, substituted benzimidazole
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 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.

Pharmacodynamic
During treatment with antisecretory medicinal products, serum gastrin increases in response to the decreased acid secretion. Also CgA increases due to decreased gastric acidity. The increased CgA level may interfere with investigations for neuroendocrine tumours.
Available published evidence suggests that proton pump inhibitors should be discontinued between 5 days and 2 weeks prior to CgA measurements. This is to allow CgA level that might be spuriously elevated following PPI treatment to return to reference range.

14. Pharmacokinetics properties

Absorption
After ingestion, pantoprazole is rapidly absorbed into the bloodstream. On average the maximum serum concentration (C_{max}) of 1 to 1.5 µg/mL (pantoprazole 20 mg tablet) or 2 to 3 µg/mL (pantoprazole 40 mg tablet) are achieved at about 2 to 2.5 hours after administration. After single and repeated administration of pantoprazole, the pharmacokinetic characteristics of pantoprazole are very similar.

Both oral and I.V. administration of pantoprazole in the dose range of 10 mg to 80 mg result in linear serum pharmacokinetics. The absolute bioavailability from the tablet was found to be about 77%. Concomitant intake of food had no relevant influence either on the AUC or on the C_{max} and, thus, bioavailability. Only the variability of the lag-time will be increased by concomitant food intake.

With pantoprazole granules, the peak serum concentration of 1.9 mg/l is reached after 2 – 2.5 hours in the fasting state. The AUC is about 5.5 mgh/l. Concomitant food intake reduces both AUC and the peak serum concentration and delays the time to peak concentration. This effect is reduced by taking pantoprazole granules 30 minutes before breakfast.

Distribution
Pantoprazole's serum protein binding is about 98%, and in keeping with this, pantoprazole has a low volume of distribution (about 0.15 l/kg) and limited tissue distribution.

Metabolism
Pantoprazole is rapidly eliminated from the circulation and extensively metabolized in the liver. Metabolism occurs via oxidation by the CYP enzyme system, predominantly by CYP2C19 and CYP3A4 (Phase I metabolism, which is saturable). Pantoprazole undergoes further biotransformation by conjugated with sulphate, which involves the cytoplasmic enzyme sulphotransferase (Phase II metabolism, which is not saturable), and which presents the main metabolism of pantoprazole.

Excretion and elimination
About 80% of the metabolites of pantoprazole are eliminated via the renal route, the rest via the feces. None of the metabolites are considered as biologically active. The main metabolite in both the serum and urine is desmethylpantoprazole, which is conjugated with sulphate. T½ of the main metabolite is about 1.5 hour (which is not much longer than that of pantoprazole, 1 hour).

Special populations

Impaired renal function

In patients with impaired renal function (including dialysis), pantoprazole showed no prolonged elimination half-life and no accumulation when compared with healthy subjects. No dose adjustments is necessary in patients with impaired renal function.

Impaired hepatic function

In comparison with healthy subjects, after oral administration of pantoprazole sodium to patients with liver cirrhosis classified as Child-Pugh A and B, serum elimination half-lives of pantoprazole increased to between 3 and 6 hours (pantoprazole 20 mg tablet) or 7 to 9 hours (pantoprazole 40 mg tablet and powder) and AUC values increased by a factor of 3 to 5 (pantoprazole 20 mg tablet) or 5 to 7-fold (pantoprazole 40 mg tablet and powder). Maximum serum concentrations, C_{max}, in these patients increased only slightly (1.3-fold after oral administration, 1.5-fold after I.V. application) relative to healthy subjects. The observed pharmacokinetic changes did not lead to relevant accumulation following once-daily dosing.

Age, gender, race

As with other clinically used PPIs, a small percentage of the population (about 3% Caucasians, 20% Asians) shows slower elimination of pantoprazole (T½ being up to 10 hours as compared with 1 hour). Such persons are known as poor metabolizers as a result of a deficiency of the CYP2C19 enzyme. In these individuals the metabolism of pantoprazole is probably mainly catalyzed 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 metabolizers than in subjects having a functional CYP2C19 enzyme (extensive metabolizers). Mean peak plasma concentrations were increased by about 60%. These findings have no implications for the posology of pantoprazole.

Results from several studies in children/adolescents from birth to 16 years indicate that the pharmacokinetics of pantoprazole is similar to those in adults when appropriately adjusted by patient weight, despite somewhat decreased clearance in patients less than 1 year old. Similar to adults, pediatric patients who were poor metabolizers of CYP2C19, exhibited reduced clearance that was more than 70% lower than the typical value.

Compared with younger subjects, slight increases in AUC and C_{max} were noted after single and repeated oral administration of pantoprazole to healthy elderly subjects (age > 65 years). However, no dose adjustment is necessary in elderly patients.

15. Incompatibilities

This medicinal product must not be mixed with other medicinal products except solvents such as sodium chloride 0.9% solution for injection or glucose 5% solution for injection.

16. Packaging

Box of 1 vial x Pantoprazole 40mg
Box of 5 vials x Pantoprazole 40mg
Box of 10 vials x Pantoprazole 40mg

17. Special precautions for disposal and other handling

Reconstituted solution:

A ready-to-use is prepared by injecting 10ml of physiological sodium chloride solution into the vial containing the powder. This solution can be administered directly. The

reconstituted solution for injection is physically and chemically stable over a period of 12 hours at 25°C. Glass container should be used for reconstitution.

Diluted solution:
The vial containing the powder is reconstituted with 10ml of sodium chloride (0.9%) solution for injection (in glass container), which is further diluted with 100ml of 0.9% sodium chloride solution for injection (in PE container) or glucose 50mg/ml (5%) solution for injection (in PE container).
The reconstituted and diluted solution of drug product thus obtained is physically compatible and chemically stable over a period of 12 hours at 25°C.
From a microbiological point of view, the product should be used immediately.
Pantoprazole should not be prepared or mixed with solvents other than those stated.
The drug 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.

18. Storage condition

Store below 30°C, protect from moisture and light.
Store the vial in the box. Take the vial out from the box just before use.

After reconstitution (in glass container), or reconstitution and dilution (in PE container), 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.

19. Shelf life

Unopened vial
24 months from the manufacturing date.

20. Date of revision

15 May 2026

21. Name and address of manufacturer

Branch of Imexpharm Corporation Binh Duong Hi-Tech Plant
Vietnam Singapore Industrial Park II,
Hoa Phu Ward, No. 21, Road No. 4,
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Commercial package insert font type & size: Times New Roman 7