For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

Pantosec IV 40 mg

(Pantoprazole for Injection)

Composition
Each vial contains:
Pantoprazole sodium sesquihydrate Ph.Eur eq.to Pantoprazole…40 mg
As sterile, freeze-dried powder for reconstitution with 10 ml of
Sodium Chloride Injection IP

Dosage Form
Intravenous Injection

Product Description
Description :Off-white powder /cake
Description of reconstituted solution :Clear colourless solution

Pharmacodynamics/Pharmacokinetics

PHARMACODYNAMICS
Proton pump inhibitors
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.
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 sulphenamide, 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 distally to the receptor level, it can inhibit gastric acid secretion irrespective of the nature of the stimulus (acetylcholine, histamine, gastrin).
Pantoprazole's selectivity is due to the fact that it can only exert 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.Pantoprazole has the same effect whether administered orally or intravenously.

PHARMACOKINETICS
General Pharmacokinetics
Terminal half-life is about 1 hour. Volume of distribution is about 0.15 L/kg, clearance is about 0.1 L/h/kg and Cmax is approximately 5.53 mg/l.Pharmacokinetics does not vary after single or repeated administration. The plasma kinetics of pantoprazole are linear after both oral and intravenous administration.
Studies with pantoprazole in humans reveal no interaction with the cytochrome P450-system of the liver. There was no induction of the P450-system seen as tested after chronic administration with antipyrine as a marker. Also, no inhibition of metabolism was observed after concomitant administration of pantoprazole with either antipyrine, caffeine, carbamazepine, diazepam, diclofenac, digoxin, ethanol, glibenclamide, metopolol, naproxen, nifedipine, phenprocoumon, phenytoin, piroxicam, theophylline, or oral contraceptives. Concomitant administration of pantoprazole with warfarin has no influence on warfarin's effect on the coagulation factors.
Pantoprazole's plasma protein binding is about 98%. The substance is almost exclusively metabolized in the liver. Renal elimination represents the major route of excretion (about 80%) for the metabolites of pantoprazole; the rest are excreted in the feces. The main metabolite in both the plasma and urine is desmethylpantoprazole which is conjugated with sulphate. The half-life of the main metabolites (about 1.5 hours) is not much longer than that of pantoprazole.
Characteristics in patients/special groups of subjects:
Although for patients with hepatic cirrhosis (classes A and B according to Child) the half-time values increased to between 7 and 9 hours and the AUC values increased by a factor of 5 to 7, the maximum plasma concentration only increased slightly by a factor of 1.5 compared with healthy subjects. As pantoprazole has a good safety profile and is well tolerated it can be given to patients with mild to moderate liver impairment. No dose reduction is required when pantoprazole is administered to patients with impaired kidney function (including dialysis patients). As with healthy subjects, pantoprazole's half-life is short. Only very small amounts of pantoprazole are dialysed. Although the main metabolite has a moderately delayed half-life (2-3 hours), excretion is still rapid and thus accumulation does not occur.A slight increase in AUC and Cmax in elderly volunteers compared with younger counterparts is also not clinically relevant.

Children
Following administration of single I.V. 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 and weight. AUC and volume of distribution were in accordance with data from adults.

Indication
Short term use for symptomatic improvemenit 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 '

Recommended Dose
PANTOSEC I.V. is for intravenous administration ONLY and must NOT be given by any other route. PANTOSEC I.V. is recommended only if oral application is not appropriate.
Duodenal ulcer, gastric ulcer, moderate and severe reflux esophagitis
The recommended intravenous dosage is one vial (40 mg pantoprazole) of PANTOSEC I.V. per day.
Long-term management of Zollinger-Ellison Syndrome and other pathological hypersecretory conditions
Patients should start their treatment with a daily dose of 80 mg PANTOSEC I.V. Thereafter, the dosage 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 dosage 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 PANTOSEC 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 PANTOSEC I.V. to the oral formulation of pantoprazole should be performed as soon as it is clinically justified.
PANTOSEC I.V. should not be reconstituted with diluents other than those stated.After preparation, the solution must be used within 12 hours and the unused portion discarded. In most patients, freedom from symptoms is achieved rapidly. As soon as oral therapy is possible, treatment with PANTOSEC I.V. should be discontinued.
Data are available on I.V. use for up to 7 days. Thereafter, oral Pantosec treatment should be administered in compliance with the approved dosage regimen.
Duodenal ulcer:
Duodenal ulcers generally heal within 2 weeks. If a 2-week period of treatment is not sufficient, healing will be achieved in almost all cases within a further 2 weeks.
Gastric ulcer:
A 4-week period is usually required for the treatment of gastric ulcers. If this is not sufficient, healing will usually be achieved within a further 4 weeks.
Gastro-esophageal Reflux:
A 4-week period is usually required for the treatment of gastro-esophageal reflux. If this is not sufficient, healing will usually be achieved within a further 4 weeks.
Elderly:
No dose adjustment is necessary in the elderly.
Patients with impaired renal function:
No dose adjustment is necessary in patients with renal impairment.
Patients with severe liver impairment:
In patients with severe liver impairment, the daily dose should be reduced to 20 mg pantoprazole. Furthermore, in these patients the liver enzymes should be monitored during PANTOSEC I.V. therapy. In case of a rise in the liver enzymes, PANTOSEC I.V. should be discontinued.
Children:
The experience in children is limited. Therefore, PANTOSEC I.V. Powder for Solution for Injection is not recommended for use in patients below 18 years of age until further data become available.

Mode of Administration
Intravenous
A ready-to-use solution is prepared by injecting 10 ml of physiological sodium chloride solution into the vial containing the dry substance. The reconstituted solution should be colourless to faintly yellow. This solution may be administered directly or may be administered after mixing with 100 ml physiological sodium chloride solution, or 5% Glucose. 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.
Pantoprazole powder for solution for injection should not be manufactured or mixed with solvents other than those stated.
The medicinal product should be administered intravenously over 2-15 minutes.
Any product that has remained in the container or the visual appearance of which has changed (e.g. if cloudiness or precipitation is observed) has to be discarded.
The contents of the vial is for single use only.

Contraindication
PANTOSEC I.V. should not be used in cases of known hypersensitivity to pantoprazole. Pantoprazole like other PPIs, should not be co-administered with atazanavir.

Warning and Precautions
The intravenous administration of pantosec i.v. is recommended only if oral application is not appropriate. pantosec i.v. is not indicated for mild gastrointestinal complaints such as nervous dyspepsia. 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. The daily dose of 40 mg pantoprazole should not be exceeded in elderly patients or in those with impaired renal function. In patients with severe liver impairment the daily dose has to be reduced to 20 mg pantoprazole. Furthermore, in these patients the liver enzymes should be monitored during pantosec i.v. therapy. In case of a rise of the liver enzymes pantosec i.v. should be discontinued. To date there has been no experience with treatment in children. '

Interaction with other Medicaments
As with other acid secretion inhibitors, changes in absorption may be observed when drugs whose absorption is pH dependent, e.g. ketoconazole, are taken concomitantly.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, PPIs, including pantoprazole, should not be co-administered with atazanavir.
Pantoprazole is metabolized in the liver via the cytochrome P450 enzyme system. Although studies have shown that pantoprazole has no significant effect on cytochrome P450, an interaction of pantoprazole with other drugs or compounds which are metabolized using the same enzyme system cannot be excluded.However, no clinically significant interactions were observed in specific tests with a number of such drugs/compounds, namely antipyrine, caffeine, carbamazepine, diazepam, diclofenac, digoxin, ethanol, glibenclamide, metoprolol, naproxen, nifedipine, phenytoin, piroxicam, theophylline and an oral contraceptive. There were also no interactions with concomitantly administered antacids.Although no interaction during concomitant administration of phenprocoumon or warfarin has been observed in clinical pharmacokinetic studies, a few isolated cases of changes in INR have been reported during concomitant treatment in the post-marketing period.

Therefore, in patients treated with coumarin anticoagulants, monitoring of prothrombin time/INR is recommended after initiation, termination or during irregular use of pantoprazole.

Pregnancy and Lactation
Clinical experience in pregnant women is limited. There is no Information on the excretion of pantoprazole into human breast milk. PANTOSEC I.V. should only be used when the benefit to the mother is considered greater than the potential risk to the foetus/baby.'

Side Effects

Frequency Organ System	Common	Uncommon	Rare	Very rare
Blood and lymphatic system				Leukopenia: Thrombocy-topenia
Gastrointestinal disorders	Upper abdominal pain; Diarrhoea; Constipation; Flatulence	Nausea/ Vomiting	Dry mouth	
General disorders and administration site conditions				Injection site thrombophle-bitis; Peripheral edema
Hepatobiliary disorders				Severe hepatocellular damage leading to jaundice with or without hepatic failure
Immune system disorders				Anaphylactic reactions including anaphylactic shock
Investigations				Increased liver enzymes (transamina-ses, γ-GT); Elevated triglycerides; Increased body temperature
Musculoskeletal, connective tissue disorders			Athralgia	Myalgia
Nervous system disorders	Headache	Dizziness; Disturbances in vision (blurred vision)		
Psychiatric disorders			Depressi-on, Hallucina-tion, Disorient-aton and confusion, especially in predispo-sed patients, as well as the aggrava-tion of these symptoms in case of pre-existence	
Renal and urinary disorders				Interstitial nephritis
Skin and sub-cutaneous tissue disorders		Allergic reactions such as pruritus and skin rash		Urticaria; Angioedema; Severe skin reactions such as Stevens Johnson Syndrome; Erythema Multi-forme; Lyell-Syndrome; Photosen-sitivity

Symptoms and Treatment of Overdose
There are no known symptoms of overdosage in man. However, pantoprazole is very specific in action and no particular problems are anticipated. Doses up to 240 mg i.v. were administered without obvious adverse effects. As pantoprazole is extensively protein bound, it is not readily dialysable. Apart from symptomatic and supportive treatment, no specific therapeutic recommendations can be made.

Incompatibilities
This medicinal product should not be manufactured or mixed with solvents other than those stated

Storage Condition
Store below 30°C.
Balance Solution Or Unused Solution To Be Discarded

Shelf Life
Pantoprazole for Injection: 24 months
Sodium Chloride Injection: 36 months
Balance Solution Or Unused Solution To Be Discarded
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.

Pack Size
Carton containing one plastic tray with 1 vial of 10 ml
and diluent of 10 ml each.

Registration Holder in Malaysia
CIPLA MALAYSIA SDN BHD
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Centre, 18 Persiaran Barat,
46 050 Petaling Jaya, Selangor, Malaysia.

Mfg By:
Cipla Ltd.
M-61, M-62 & M-63 Verna Industrial Estate
Verna Goa, INDIA

Date of Revision
September 2019

Cipla

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PACKAGING DEVELOPMENT

Product Name: Pantosec IV Injecion

Material No.: | **Version:** 01 | **Item:** Leaflet | **Co-ordinator:** Vinod V. | **Artist:** Manish | **Date:** 06-09-2019

Colours: Black
BLUE WOOL TEST VALUE 5-6 (LIGHT FASTENING DATA)

INK: Oil based Ink from DIC OR MICRO

Design: Unfolded

Supersedes/Reference: 21066587 | **Software:** Illustrator CC

Fonts: ------

Links: ------

Actual Size: 140 x 220 mm | **Size after folding:** ---- | **Pharmacode:** –_MINI | **Grain Direction :** Parallel to length | **Screen : # —**

Material: 54 GSM Maplitho Paper

Varnish: | **Artwork Print Size:** ☐ actual ☐ scaled

Path:D:\Manish\April 2019 to March 2020\Vinod V\MalaysialPantosec IV Injecion Leaflet Malaysia.ai

	Checked by	Artist	Cordinator	file loaded in Server	Section Head
	Pharma Code	☐☐☐☐☐☐☐	☐☐☐☐☐☐☐		
	2D Code				
	QR Code				
	Bar Code				
	Artwork				
	Spell check				

- **Instructions / Remark:** --------
- Any deviation must be brought to the notice of packaging development co-ordinator immediately.
- For any clarification, please contact packaging development co-ordinator immediately.
- NO CHANGES IN ARTWORK SHOULD BE DONE BY THE PRINTER
- The printer should verify the e-proof against the approved artwork before submitting for approval and the e-proof should have printer details .