PANTOPRAZOLE SODIUM

REDUCTAZID

40 mg Powder for Solution for Injection (IV)
Proton Pump Inhibitor

℞

FORMULATION
Each vial contains:
Pantoprazole (as sodium), USP..... 40 mg

INDICATIONS
Gastroesophageal reflux disease associated with a history of erosive esophagitis
Pantoprazole for injection is indicated for short-term treatment (7 to 10 days) of adult patients with gastroesophageal reflux disease (GERD) and a history of erosive esophagitis.

Safety and efficacy of pantoprazole for injection as treatment of patients with GERD and a history or erosive esophagitis for more than 10 days have been demonstrated.

Pathological hypersecretion including Zollinger-Ellison Syndrome
Pantoprazole for injection is indicated for the treatment of pathological hypersecretory conditions including Zollinger-Ellison syndrome in adults.

DOSAGE AND ADMINISTRATION
Parenteral drug products should be inspected visually for particulate matter and discoloration prior to and during administration whenever solution and container permit.

Parenteral routes of administration other than intravenous are not recommended.

Pantoprazole for injection may be administered intravenously through a dedicated line or through a Y-site. The intravenous line should be flushed before and after administration of pantoprazole for injection with either 5 % Dextrose injection, USP, 0.9 % Sodium Chloride Injection, USP, or Lactated Ringer's Injection, USP. When administered through a Y-site, pantoprazole for injection is compatible with the following solutions: 5 % Dextrose Injection, USP, 0.9 % Sodium Chloride Injection, USP, or Lactated Ringer's Injection, USP.

Midazolam HCl has been shown to be incompatible with Y-site administration of pantoprazole for injection. Pantoprazole for injection may not be compatible with products containing zinc. When pantoprazole for injection is administered through Y-site, immediately stop use if precipitation or discoloration occurs.

Gastroesophageal reflux disease associated with a history of erosive esophagitis

Recommended Dosage

The recommended adult dose is 40 mg pantoprazole given once daily by intravenous infusion for 7 to 10 days.

Administration and preparation instructions
Data on the safe and effective dosing for condition other than those described (see Indications and Usage) such as a life-threatening upper gastrointestinal bleeds, are not available. PANTOPRAZOLE 40 mg once daily does not raise gastric pH to levels sufficient to contribute to the treatment of such life-threatening conditions.

Fifteen minutes infusion
Pantoprazole for injection should be reconstituted with 10 mL 0.9 % Sodium Chloride Injection, USP, and further diluted (admixed) with 100 mL of 5 % Dextrose Injection, USP, 0.9 % Sodium Chloride Injection, USP, or Lactated Ringer's Injection, USP, to a final concentration of approximately 0.4 mg/mL. The reconstituted solution may be stored up to 6 hours at room temperature prior to further dilution. The admixed solution may be stored at room temperature and must be used within 24 hours from the time of initial reconstitution. Both the reconstituted solution and the admixed solution do not need to be protected from light.

PANTOPRAZOLE for injection admixtures should be administered intravenously over a period of approximately 15 minutes at a rate of approximately 7 mL/min.

Two minutes infusion
Pantoprazole for injection should be reconstituted with 10 mL of 0.9 % Sodium Chloride Injection, USP, to a final concentration of approxiamately 4 mg/mL. The reconstituted solution may be stored for up to 24 hours at room temperatures prior to intravenous infusion and does not need to be protected from light. PANTOPRAZOLE for injection should be administered intravenously over a period of at least 2 minutes.

Pathological hypersecretion including Zollinger-Ellison syndrome

Recommended Dosage
The dosage of PANTOPRAZOLE for injection in patients with pathological hypersecretory conditions including Zollinger-Ellison syndrome varies with individual patients, The recommended adult dosage is 80 mg intravenously every 12 hours. The frequency of dosing can be adjusted to individual patient's needs based on acid output measurements. In those patient who need a higher dosage, 80 mg intravenously every 8 hours is expected to maintain acid output below 10 mEq/h. Daily doses higher than 240 mg or administered for more than 6 days have not been studied. Transition from oral to intravenous and from intravenous to oral formulations of gastric acid inhibitors should be performed in such a manner to ensure continuity of effect of acid suppression. Patients with Zollinger-Ellison syndrome may be vulnerable to serious clinical complications of increased acid production even after a short period of loss effective inhibition.

Administration and preparation instructions

Fifteen minutes infusion
Each vial of PANTOPRAZOLE for injection should be reconstituted with 10 mL of 0.9 % Sodium Chloride Injection, USP, The contents of two vials should be combined and further diluted (admixed) with 80 mL of 5 % Dextrose Injection, USP, 0.9 % Sodium Chloride Injection, USP, or Lactated Ringer's Injection, USP to a total volume of 100 mL with a final concentration of approximately 0.8 mg/mL. The reconstituted solution may be stored for up to 6 hours at room temperature prior to further dilution. The admixed solution may be stored at room temperature and must be used within 24 hours from the time of initial reconstitution. Both the reconstituted solution and the admixed solutoin do not need to be protected from light.

PANTOPRAZOLE for injection should be administered intravenously over a period of approximately 15 minutes at a rate of approximately 7 mL/min.

Two minutes infusion
PANTOPRAZOLE for injection should be reconstituted with 10 mL of 0.9 % Sodium Chloride Injection, USP, per vial to a final concentration of approximately 4 mg/mL. The reconstituted solution may be stored for up to 24 hours at room temperature prior to intravenous infusion and does not need to be protected from light. The total volume from both vials should be administered intravenously over a period of at least 2 minutes.

CONTRAINDICATIONS
Pantoprazole is contraindicated in patients with known hypersensitivity reactions including anaphylaxis to the formulation or any substituted benzimidazole.

WARNING AND PRECAUTIONS

Implications of symptomatic response
Symptomatic response to therapy with pantoprazole does not preclude the presense of gastric malignancy.

Hypersensitivity and severe skin reactions
Anaphylaxis and other serious reactions such as erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis (TEN) have been reported with use of intravenous pantoprazole. These may require emergency medical treatment.

Injection site reactions
Thrombophlebitis was associated with administration of intravenous pantoprazole.

Clostridium difficile associated diarrhea
Published observational studies suggest that PPI therapy like pantoprazole maybe 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.

Bone fracture
Several published observational studies suggest that proton pump inhibitor (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-dose, defined as multiple daily doses, and long-term PPI therapy (a year or longer). Patients should use the lowest dose and shortest duration of PPI therapy appropriate to the condition being treated. Patients at risk for osteoporosis-related fractures should be managed according to established treatment guidelines.

Hepatic effects
Mild, transient transaminase elevations have been observed in clinical studies. The clinical significance of this finding in a large population of subjects administered intravenous pantoprazole is unknown.

Hypomagnesemia
Hypomagnesemia, symptomatic and asymptomatic, has been reported rarely in patients treated with PPIs for at least three months, and in most cases after a year of therapy. Serious adverse events include tetany, arrhythmias, and seizures. In most patients treatment of hypomagnesemia required magnesium replacement and discontinuation of PPI.

For patients expected to be on prolonged treatment or who take PPIs with medications such as digoxin or drugs that may cause hypomagnesemia (e.g., diuretics), health care professionals may consider monitoring magnesium levels prior to initiation of PPI treatment and periodically.

Interference with urine screen for THC
May produce false-positive urine screen for THC (tetrahydrocannabinol)

Concomitant use of pantoprazole with methotrexate
Literature suggest that concomitant use of PPIs with methotrexate (primarily at high dose; see methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or its metabolite, possible leading to methotrexate toxicities. In high-dose methotrexate administration, a temporary withdrawal of the PPI may be considered in some patients.

ADVERSE DRUG REACTIONS
Postmarketing experience
The following adverse reactions have been identified during post approval use of pantoprazole. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a casual relationship to drug exposure.

These adverse reactions are listed below by body system:

General disorders and administration conditions: asthenia, fatigue, malaise
Immune system disorders: anaphylaxis (including anaphylactic shock)
Investigations: weight changes
Skin and subcutaneous tissue disorders: severe dermatologic reactions (some fatal), including erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis (TEN), and angioedema (Quincke's edema)
Musculoskeletal disorders: rhabdomyolysis, bone fracture
Renal and urinary disorders: interstitial nephritis
Hepatobiliary disorders: hepatocellular damage leading to jaundice and hepatic failure
Psychiatric disorder: hallucinations, confusion, insomnia, somnolence
Metabolism and nutritional disorders: hyponatremia, hypomagnesemia
Infections and Infestations: Clostridium difficile associated diarrhea
Hematologic: pancytopenia, agranulocytosis
Nervous: ageusia, dysgeusia

DRUG INTERACTIONS

Interference with antiretroviral therapy
Concomitant use of atazanavir or nelfinavir with proton pump inhibitors is not recommended. Coadministration of atazanavir or nelfinavir with proton pump inhibitors is expected to substantially decrease atazanavir or nelfinavir plasma concentrations and may result in a loss of therapeutic effect and development of drug resistance.

Coumarin anticoagulants
There have been postmarketing reports of increased INR and prothrombin time in patients receiving proton pump inhibitor, including pantoprazole and warfarin concomitantly. Increases in INR and prothrombin time may lead to abnormal bleeding and even death, Patients treated with proton pump inhibitors and warfarin concomitantly should be monitored for increases in INR and prothrombin time.

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 for which gastric pH can affect bioavailability
Pantoprazole causes long-lasting inhibition of gastric acid secretion, therefore pantoprazole may interfere with absorption of drugs where gastric pH is an important determinant of their bioavailability (e.g., ketoconazole, ampicillin esters, iron salts, and digoxin).

False positive urine test for THC
There have been reports of false positive urine screening test for tetrahydrocannabinol (THC) in patients receiving proton pump inhibitors including pantoprazole. An alternative confirmatory method should be considered to verify positive results.

Methotrexate
Case reports, published population pharmacokinetic studies, and retrospective analyses suggest that concomitantly administration of PPIs and methotrexate (primarily at high dose; see methotrexate prescribing information) may elevate and prolong serum levels of methotrexate and/or metabolite hydroxymethotrexate. However, no formal drug interaction studies of methotrexate with PPIs have been conducted.

USE IN SPECIFIC POPULATIONS

Pregnancy
Teratogenic Effects

Pregnancy Category B
There are no adequate and well-controlled studies in pregnant women because animal reproduction studies are not always predictive of human response, this drug should be used in pregnancy only if clearly needed.

Nursing Mothers
Pantoprazole and its metabolites are excreted in milk of rats. Pantoprazole excretion in human milk has been detected in a study of a single nursing mother after a single 40 mg oral dose. The clinical relevance of this findings is not known. Many drugs which excreted in human milk have a potential for serious adverse reactions in nursing infants. Based on the potential for tumorigenicity shown for pantoprazole in rodent carcinogenicity studies, a decision should be made whether to discontinue nursing or to discontinue the drug taking into account the benefit of the drug to the mother.

Pediatric use
Safety and effectiveness of pantoprazole in pediatric patients have been established.

Geriatric use
The incidence rates of adverse events and laboratory abnormalities in patients aged 65 years and older were similar to those associated with patients younger than 65 years of age.

Gender
No gender-related differences in the safety profile of intravenous pantoprazole were seen involving men and women with erosive esophagitis associated with GERD. The incidence rates of adverse reactions were also similar for men and women.

Hepatic impairment
Doses higher than 40 mg/day have not been studies in patients with hepatic impairment.

OVERDOSAGE
Experience in patients taking very high doses of pantoprazole (>20 mg) is limited. Adverse events seen in spontaneous reports of overdose generally reflect the known safety profile of pantoprazole.

Pantoprazole is not removed by hemodialysis. In case of overdosage, treatment should be symptomatic and supportive.

The symptoms of acute toxicity were hypoactivity, ataxia, hunched sitting, limb-splay, lateral position, segregation, absence of ear reflex, and tremor.

AVAILABILTY
USP Type I 10 ml clear glass vial (Box of 1's)

CAUTION
Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

STORAGE CONDITION
Store at temperatures not exceeding 30°C.

"For suspected adverse drug reaction, report to the FDA: www.fda.gov.ph.
Seek medical attention immediately at the first sign of any adverse drug reaction."

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