PAMIDRONATE DISODIUM INJECTION
For IV Infusion

DESCRIPTION
Pamidronate Disodium Injection is a bone resorption inhibitor available in 30 mg and 90 mg sterile vials for intravenous administration.

CLINICAL PHARMACOLOGY
Pamidronate disodium is a pyrophosphate analog that inhibits osteoclastic bone resorption, resulting in reductions of bone turnover. It is therefore used to treat a variety of bone-related conditions, including hypercalcemia of malignancy, osteoporosis, and Paget's disease.

PHARMACOKINETICS
Pamidronate is rapidly cleared from the blood and most of the dose is eliminated from the body by the kidneys. In rats given 10 mg/kg bolus injections of radiolabeled pamidronate disodium, approximately 30% of the compound was found in the liver (4 hrs) while about 70% was found in the urine (24 hrs) with renal clearance of about 200 mL/min.

Metabolism
The mean ± SD body retention of pamidronate was calculated to be 54 ± 16% of the dose over 120 hours.

Renal Insufficiency
Excessive accumulation of pamidronate in renally impaired patients has been reported. Given the recommended dose, 90 mg infused over 4 hours, patients with severe renal impairment, defined as creatinine clearance below 30 mL/min, should be monitored closely for signs of toxicity, including generalized bone pain.

Contraindications
Pamidronate disodium injection is contraindicated in patients with a history of hypersensitivity to pamidronate or any other component of the injection and in patients with severe renal impairment (creatinine clearance < 30 mL/min).

ADVERSE REACTIONS
Pamidronate disodium injection may cause muscle and bone pain, fatigue, nausea, headache, constipation, and dizziness.

INDICATIONS AND USAGE
Pamidronate Disodium Injection is indicated for the treatment of hypercalcemia of malignancy. It is also used in the treatment of Paget's disease of bone and to increase bone mineral density and decrease bone pain in postmenopausal women with osteoporosis who are at high risk of fracture.

PRECAUTIONS
Patients with renal dysfunction should be monitored closely for signs of toxicity, including generalized bone pain. Patients should be hydrated adequately to treat hydration status, and the dose should be reduced in patients with severe renal impairment.

DRUG INTERACTIONS
Pamidronate is a bone resorption inhibitor that may interact with other drugs that also inhibit bone resorption.

CONTRAINdications
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WARNINGS
Patients with renal dysfunction should be monitored closely for signs of toxicity, including generalized bone pain. Patients should be hydrated adequately to treat hydration status, and the dose should be reduced in patients with severe renal impairment.

Drug Interactions
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References
The following table lists the adverse experiences considered to be treatment-related during comparative, controlled U.S. trials. Many of these adverse experiences may have been related to the underlying disease state.

At least 15% of patients treated with pamidronate disodium for hypercalcemia of malignancy also experienced the following adverse events during a clinical trial:

- Convulsions
- Anxiety
- Rales
- Dyspnea
- Myalgia
- Tachycardia
- Cardiac failure
- Psychosis
- Hypertension
- Abnormal liver function
- Hypophosphatemia
- Anorexia
- Nausea
- Vomiting
- Abdominal pain

At least 10% of all pamidronate disodium-treated patients with Paget's disease also experienced the following adverse experiences during clinical trials:

- Headache
- Hypocalcemia
- Hypernatremia
- Hyperkalemia
- Hematuria

The optimal duration of therapy is not yet known; however, in a study of patients with hypercalcemia, final analyses performed after 21 months of treatment revealed several benefits (see Clinical Studies). In a study of patients with Paget's disease, treatment should be continued until clinical benefit is observed or drug therapy is no longer effective.

Some of the adverse experiences listed in this section are the same as those presented in WARNINGS. These experiences are included here to document their frequency of occurrence to facilitate comparison with other medications and to document the presence of symptoms that may be relevant to specific adverse experiences.

Pregnancy: Teratogenic Effects: Pregnancy Category D

Pamidronate disodium is contraindicated in patients who have a history of hypersensitivity to the drug or to any of its components. The drug is contraindicated in patients who are expected to have a protracted or severe reaction to the drug, including patients who have a history of severe reactions to intravenous bisphosphonates, including pamidronate disodium. No animal studies have been performed to determine if pamidronate disodium is teratogenic. Therefore, it is contraindicated in women of childbearing potential who are unable to exclude pregnancy. It is not known whether pamidronate disodium is excreted in human milk. The manufacturer recommends that women receiving pamidronate disodium should not breastfeed.

Pamidronate disodium should be given in a slow intravenous infusion. In patients with dehydration, intravenous hydration with a normal saline solution should be administered in the intravenous line when pamidronate disodium is given. The drug should not be administered by the intramuscular or subcutaneous route. Formulation is not intended for oral administration. Intravenous administration of the drug is recommended for patients who require a rapid onset of action.

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