KATHY WILKINSON, RN, BSN, OCN®
ASSOCIATE EDITOR

Zoledronic Acid

Angie Osborne, RN, OCN®

Drug name: Zoledronic acid is manufactured as Zometa® by Novartis Pharmaceuticals Corporation in Basle, Switzerland, for Novartis Pharmaceuticals Corporation in East Hanover, NJ.

Classification: Bisphosphonate

Action: Zoledronic acid inhibits the resorption of mineralized bone and cartilage. It inhibits the increased osteoclastic activity and skeletal calcium that is induced by stimulatory factors released by malignant tumors.

Indications: Zoledronic acid is indicated for the treatment of hypercalcemia, multiple myeloma, and osteolytic metastases in solid tumors. Clinical trials are ongoing for zoledronic acid use in osteoporosis, secondary to osteoarthritis and Paget's disease.

Metabolism: Zoledronic acid does not undergo biotransformation in vivo. Less than 3% of the administered intravenous dose was found in the feces, with the balance either recovered in the urine or taken up by bone. The drug is excreted unchanged in the urine.

Excretion: Renal

Half-life: Zoledronic acid's early distribution half-life is 0.23 hours, early elimination half-life is 1.75 hours, and terminal elimination half-life is 167 hours, with low plasma concentrations observed up to 28 days post-dose.

Effects on blood counts: No adverse hematologic effects were reported. Mild anemia was reported in clinical trials.

Adverse reactions and effects: Adverse reactions to zoledronic acid usually are mild, transient, and similar to those of other bisphosphonates. Fever is the most common reaction reported. Patients also may experience flu-like syndrome, such as fever, chills, bone and joint pain, and myalgias. The drug also may cause some gastrointestinal reactions, such as nausea and vomiting. Monitoring laboratory abnormalities is important because zoledronic acid can cause low calcium, phosphorus, potassium, and magnesium levels. Renal toxicity has been reported; serum creatinine should be monitored prior to each dose and treatment withheld if serum creatinine increases by 0.5 mg/dl in patients with normal baseline or 1.0 mg/dl in patients with an abnormal baseline level.

Precautions: Because of the risk of a clinically significant reduction in renal function, which may progress to renal failure, single doses of zoledronic acid should not exceed 4 mg. In addition, the duration of the infusion should be no less than 15 minutes. In clinical trials, 4 mg of zoledronic acid given as a five-minute infusion carried an increased risk of renal toxicity.

Interactions: Zoledronic acid must be used with caution with loop diuretics (to avoid hypocalcemia) and aminoglycosides (they lower calcium if given over a long period of time). Concurrent use of drugs known to cause renal toxicity should be avoided. Patients with multiple myeloma receiving thalidomide are at increased risk for renal dysfunction when taking zoledronic acid.

Route and dosage: The maximum recommended dose of zoledronic acid is 4 mg given as a single-dose IV infusion over no less than 15 minutes. Patients may be considered for retreatment with 4 mg of zoledronic acid but must wait at least seven days to allow for full response to the initial dose when used for hypercalcemia. Zoledronic acid 4 mg is administered every three to four weeks in patients with multiple myeloma or those with bone metastases from solid tumors.

Dilution and reconstitution: Zoledronic acid is reconstituted by adding 5 ml of sterile water for injection to each vial. The 4 mg dose must be further diluted in 100 ml of sterile 9% sodium chloride or 5% dextrose injection.

Contraindications: Zoledronic acid is contraindicated in patients with renal impairment or failure and patients experiencing fluid and electrolyte imbalance (i.e., hypovolemia, hypocalcemia, hypomagnesemia, hypophosphatemia). The U.S. Food and Drug Administration classified zoledronic acid in the pregnancy risk category C; thus, the drug should be avoided during pregnancy. Whether zoledronic acid is excreted in breast milk is unknown; therefore, breastfeeding should be avoided. Bisphosphonates have been associated with acute bronchospasm in patients with aspirin-sensitive asthma and phosphonate hypersensitivity.

Stability: If not used immediately after reconstitution, the solution should be refrigerated at 2°–8°C (36°–46°F). If refrigerated, return the solution to room temperature before administration. The total time between reconstitution, dilution, and administration must not exceed 24 hours.

Premedication: None

Nursing implications: Nurses administering zoledronic acid should do the following.

- Review all baseline laboratory tests, including complete blood count, serum calcium, serum creatinine, blood urea nitrogen, serum electrolytes, serum magnesium, and phosphate.
- Measure serum creatinine before administering each dose of zoledronic acid, and withhold treatment if renal deterioration occurs. In clinical studies, renal deterioration was defined as follows.
  – For patients with normal baseline creatinine, an increase of 0.5 mg/dl; for patients with abnormal baseline creatinine, an increase of 1.0 mg/d (Zoledronic acid treatment was resumed only when the creatinine returned to within 10% of the baseline value.)

Angie Osborne, RN, OCN®, is an oncology nurse with the Hematology Oncology Centers of the Northern Rockies in Billings, MT. *(Mention of specific products and opinions related to those products do not indicate or imply endorsement by the* Clinical Journal of Oncology Nursing *or the Oncology Nursing Society.)*

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