Once-Yearly Reclast Approved for Osteoporosis

BY ELIZABETH MECHCATIE
Senior Writer

The intravenous bisphosphonate zoledronic acid (Reclast) has been approved as the first treatment for postmenopausal osteoporosis that is administered once a year.

The approved dosage of zoledronic acid is a single 5-mg infusion given intravenously, over no less than 15 minutes, annually. The approval was announced in August by the drug's manufacturer, Novartis Pharmaceuticals Corporation.

The 5-mg formulation of intravenous zoledronic acid was first approved earlier this year as a treatment for Paget disease. Zoledronic acid has been available in a 4-mg formulation (Zometa) for oncology indications, which is still available and should not be used in a patient taking Reclast.

Like other bisphosphonates, zoledronic acid inhibits osteoclast-mediated bone resorption. Daily, weekly, or monthly dosing schedules for oral bisphosphonate drugs previously have been approved by the Food and Drug Administration. An injectable form of the bisphosphonate ibandronate (Boniva) is approved for use every 3 months for postmenopausal osteoporosis.

The average wholesale acquisition price for each zoledronic acid 5-mg dose is $1,041.00, but the retail price may vary, a Novartis spokesperson said.

Approval for the osteoporosis indication was based on a 3-year, international study of more than 7,700 women with postmenopausal osteoporosis, the Health Outcomes and Reduced Incidence with Zoledronic Acid Once Yearly (HORIZON) Pivotal Fracture Trial.

The study, which was published in May, found that women who received an annual 5-mg intravenous infusion of zoledronic acid had a 70% lower risk of vertebral fractures over a 3-year period, compared with women who were taking placebo.

Vertebral fracture occurred in 3.3% of the zoledronic acid group and 10.9% of the placebo group (N. Engl. J. Med. 2007;356:1809-22).

Hip fracture occurred in 1.4% of the zoledronic acid group and 2.5% of the placebo group, which represented a 41% reduction in the risk of hip fracture with active treatment.

Compared with placebo, zoledronic acid treatment also was associated with a significant reduction in nonvertebral fractures, clinical fractures, and clinical vertebral fractures, and significant improvements in bone mineral density and bone metabolism markers. These differences between groups were all statistically significant.

"Given the relatively poor adherence to oral bisphosphonate therapy in clinical practice, annual infusion of zoledronic acid may provide a promising approach to reducing fracture risk," the study authors concluded.

The study was supported by Novartis, and two authors were from Novartis.

"This is the first study where we have evidence for [a reduction in] spine, hip, and non-vertebral fractures all in the same trial," Dr. Nelson B. Watts, director of the University of Cincinnati Bone Health and Osteoporosis Center, said in an interview. Dr. Watts, one of the investigators in the trial, said that based on these efficacy data, he ranks this drug with the bisphosphonates alendronate (Fosamax) and risedronate (Actonel), which also have been shown to reduce the risks of these three significant fracture types.

Dr. Watts disclosed that he is a consultant to Novartis.

He attributes part of the drug's effectiveness to compliance. "Once the patients receive the dose, they have at least a year's worth of drug on board," he said, noting that one of the problems with treating silent diseases like osteoporosis is that a substantial proportion of patients stop taking the drug within 6-7 months of starting treatment for the disease.

Dr. Watts said that about one-third of patients have an acute phase response, with a fever, muscle aches, and other flu-like symptoms, but if they are premedicated with acetaminophen or ibuprofen, they are less likely to have those symptoms, or the symptoms, if they occur, are less severe.

This is also a first-dose phenomenon, so whether patients do or do not have these symptoms with the first dose, they are unlikely to experience the symptoms with subsequent doses, he added. ■