

# Once-Yearly Intravenous Formulation of Zoledronic Acid Approved by the FDA

EAST HANOVER, N.J., Aug. 17 - Reclast® (zoledronic acid) Injection has been approved by the US Food and Drug Administration as the first and only once-yearly medicine for postmenopausal osteoporosis, offering an important new approach to the treatment of a bone disease affecting eight million women in the US(1).

Unlike oral bisphosphonate therapies that have to be taken daily, weekly or monthly, Reclast® is given as a once-yearly 15-minute intravenous (IV) infusion. This means with a single treatment a patient can receive a full year's protection against the effects of osteoporosis -- a disorder that causes bones to break easily.

"The fact that Reclast® is highly effective and can be administered once-yearly represents a major milestone in the treatment of postmenopausal osteoporosis," said Felicia Cosman, MD, Professor of Clinical Medicine, Columbia University.

"For the first time we can ensure women receive a full year of the treatment they need to protect their bones," said Dr. Cosman.

The US approval comes a few weeks after the Committee for Medicinal Products for Human Use (CHMP) issued a positive opinion recommending approval for the medicine in the European Union, under the brand name Aclasta®. The European Commission generally follows the CHMP's recommendations and is expected to issue a final decision within three months.

The regulatory submissions were based on efficacy and safety data from a three-year Pivotal Fracture Trial, showing that Reclast® increases bone strength and reduces fractures in areas of the body typically affected by osteoporosis, including the hip, spine and non-spine (i.e. hip, wrist, arm, leg, rib). Reclast® is the only treatment proven to reduce fractures across all of these key sites.

In this study involving more than 7,700 women, Reclast® reduced the risk of spine fractures by 70% and hip fractures by 41% (The New England Journal of Medicine, May 3, 2007)(2). The reduction in spine fractures was sustained over three years (60% in

year one, 71% in year two, and 70% in year three). Bone mineral density increased significantly in the spine by 6.7% and the hip by 6% in women on Reclast® compared to placebo(2).

"Reclast® has shown significant efficacy in protecting women against fractures in all the common osteoporotic fracture sites, while demonstrating a favorable safety profile," said James Shannon, MD, Global Head of Development at Novartis Pharma AG. "It is our hope that this innovative once-yearly dosing regimen will have a positive impact on the management of this potentially devastating condition."

The need for effective treatments is pressing, with one out of every two women over the age of 50 suffering an osteoporotic fracture in her lifetime(1). The disease is responsible for 1.5 million fractures in the US every year(1), some of which can have severe consequences. Approximately 20% of women over the age of 50 who suffer a hip fracture will die within one year(1).

Osteoporotic fractures are responsible for an estimated 800,000 emergency room visits, 500,000 hospitalizations, 180,000 nursing home placements, and 2.6 million physician visits in the US each year(3), costing the healthcare system approximately \$12.2 to 17.9 billion annually(3).

"Osteoporosis is a serious disease affecting millions of people in this country," said Leo Schargorodski, executive director of the National Osteoporosis Foundation (NOF). "NOF welcomes new FDA approved treatment options, such as Reclast®, that give patients a choice when it comes to taking their osteoporosis therapy."

Reclast®/Aclasta® is approved in more than 60 countries, including the US, Canada and the EU for the treatment of Paget's disease, the second most common metabolic bone disorder. Additional studies are ongoing to examine the use of Reclast® to prevent fractures following a hip fracture in men and women, treatment of corticosteroid-induced osteoporosis, and male osteoporosis.

The active ingredient in Reclast® is zoledronic acid, which is also available in a different dosage under the brand name Zometa® (zoledronic acid 4 mg) Injection for use in certain oncology indications.

Reclast® is contraindicated in patients with hypocalcemia (low blood calcium) and those who are allergic to zoledronic acid. Reclast® contains the same active ingredient found in Zometa. Patients already being treated with Zometa should not be treated with Reclast®. Reclast® should not be used during pregnancy because of potential harm to the fetus. Reclast® is not recommended for use in patients with severe renal impairment (creatinine clearance <35 mL/min) and infusion time should not be less than 15 minutes.

The most common side effects associated with Reclast® are fever; pain in the muscles, bones or joints; flu-like symptoms; and headache. These symptoms usually occur within the first three days following Reclast® administration and usually resolve within 3 to 4 days of onset but resolution could take up to 7 to 14 days. Patients have reported severe bone, joint and/or muscle pain after using bisphosphonates. Osteonecrosis of the jaw (ONJ) has been reported rarely in postmenopausal osteoporosis patients treated with bisphosphonates. A routine oral examination should be performed by the prescriber prior to initiation of bisphosphonate treatment. Hypocalcemia may occur with Reclast® therapy. In the Pivotal Fracture Trial an increased number of cases of serious atrial fibrillation were observed in women given Reclast® compared to those on placebo (1.3% vs. 0.4% respectively)(2). The timing of these events suggest that they were not related to the acute infusion. This finding has not been observed in other zoledronic acid clinical studies and in post-marketing experience from more than 1.5 million patients treated with Zometa.

All patients with Paget's disease should receive 1500 mg of calcium in divided doses and 800 IU of vitamin D daily, particularly in the two weeks following Reclast® administration. It is recommended that patients with postmenopausal osteoporosis take calcium and vitamin D supplements, if dietary intake is not sufficient.

For more information about Reclast®, visit [www.Reclast.com](http://www.Reclast.com) or call 866-RECLAST (866-732-5278).

Source: Food and Drug Administration