

*Editors' note: This ACR Hotline was contributed by Drs. Oscar Gluck and Michael Maricic.*

## **Teriparatide (Forteo™) for the Treatment of Osteoporosis**

### **Introduction:**

On November 26, 2002, the U.S. Food and Drug Administration (FDA) approved teriparatide. The drug, a portion of human parathyroid hormone (PTH), was approved for the treatment of osteoporosis in postmenopausal women who are at high risk for having a fracture, and also to increase bone mass in men with primary or hypogonadal osteoporosis who are at high risk for fracture. Teriparatide is the first anabolic agent (i.e., it stimulates new bone formation) approved by the Food and Drug Administration for use in men and in postmenopausal women with osteoporosis. Unfortunately, when media outlets and news organizations picked up the story of teriparatide's approval, several ran stories about "a cure for osteoporosis." All other current available pharmacological agents for osteoporosis, e.g., the bisphosphonates, are antiresorptive medications. These other drugs have been shown to decrease the risk of fragility fractures.

### **Background:**

Endogenous 84 amino-acid parathyroid hormone (PTH) is a primary regulator of bone and mineral metabolism. The skeletal effects of parathyroid hormone depend upon the pattern of exposure. High dose chronic release of this hormone leads to bone resorption and bone loss (hyperparathyroidism); in contrast, once daily administration of recombinant (1-34) PTH or teriparatide preferentially stimulates new bone formation of trabecular and cortical bone.

### **Summary of clinical trials:**

A multicenter double blind placebo control study of once daily subcutaneous injection of teriparatide included 1637 PMO women with osteoporosis<sup>1</sup>. Ninety percent of patients had one or more vertebral fractures at baseline. The median exposure to teriparatide in this study was 19 months. Teriparatide (20ug/day) taken with calcium and vitamin D decreased the risk of subsequent vertebral fracture by 65% (95% CI) (P < 0.001). Vertebral fracture rates over the 19 months of the study were 136, 49, and 30 per 1000 patient years for the placebo, 20 ug, and 40 ug groups respectively. The study was not powered to determine hip fracture risk reduction, but the risk of any nonvertebral fracture was decreased by 53% (P < 0.05). In men with primary or hypogonadal osteoporosis, teriparatide (20 ug/day) increased bone mineral density with a mean percentage change from baseline to endpoint of 5.9% at the lumbar spine and 1.5% at the femoral neck with a P < 0.001 and P < 0.05 compared with placebo respectively.

### **Indications:**

Teriparatide is indicated for the treatment of postmenopausal women who are at high risk for fractures. High risk includes patients with previous fragility fractures, significant low bone mass and/or those patients who are intolerant or unresponsive to other available therapies. Teriparatide is also indicated for men with primary or hypogonadal osteoporosis at high risk for fracture to increase bone mass. High risk include men with fragility fracture, multiple risk factors for fracture, or those who have failed or are intolerant to previous osteoporosis therapy.

### **Contraindications:**

Children or young adults with open epiphyses, pregnant females, patients with hyperparathyroidism, Paget's disease of bone, osteomalacia, end-stage renal disease, primary or metastatic bone cancer, active nephrolithiasis or unexplained elevation of serum calcium or alkaline phosphatase prior to initiation of therapy. Radiation therapy involving the skeleton excludes a patient from treatment with teriparatide. Patients with metabolic bone diseases other than osteoporosis should not receive teriparatide.

**Warnings:**

In male and female rats teriparatide caused a dose and duration dependent increased incidence of osteosarcoma. The effect was observed at systemic exposures ranging from 3 to 60 fold times the potential exposure of humans at the therapeutic 20 ug dose.

**Adverse events:**

Adverse events associated with teriparatide were reported as mild and generally did not require discontinuation of therapy. During clinical trials there were increased dizziness and leg cramps.

**Practical issues:**

The safety and efficacy of teriparatide has not been evaluated beyond 2 years of treatment. Consequently use of the drug for more than 2 years is not recommended. Baseline laboratory evaluation of patients to be considered for this therapy generally includes serum creatinine, calcium, phosphorus, alkaline phosphatase and 25-OH vitamin D levels. Abnormalities in these tests should be appropriately evaluated. Although there is increase or stabilization of bone mineral density with the use of antiresorptive medications following teriparatide exposure, the effect of sequential management of osteoporosis with first antiresorptives (alendronate, risedronate or raloxifene) followed by teriparatide is as yet not known. Combination therapy using alendronate or risedronate with teriparatide is now in clinical trials.

**Dose/Use :**

20 ug SQ daily for up to 24 months. Each teriparatide pen can be used for up to 28 days and then discarded. It is stored under refrigeration at 36-46 degrees F (2-8 degrees Centigrade) at all times.

**Cost:** The Average Wholesale Price (AWP) of teriparatide is \$7,592 per year.

**Monitoring of patients on teriparatide:**

No specific laboratory tests must be performed for monitoring. If hypercalcemia is suspected, serum calcium should be drawn 16-24 hours after the previous dose. Monitoring bone density with DXA should be periodically performed. Biochemical markers of both bone formation and resorption increase after a few months of therapy.

**Bottom Line:**

- Teriparatide is indicated for osteoporosis patients at high risk of fragility fractures.
- The effect of sequential use of an antiresorptive medication followed by teriparatide is not known.
- Exclusion of other metabolic bone diseases different from osteoporosis is essential prior to the use of teriparatide.
- As yet, there are no guidelines for the role of teriparatide in the treatment of osteoporosis and fractures relative to other currently available therapies.

-- Oscar S Gluck, MD, Clinical Professor of Medicine, University of Arizona, Director Arizona Rheumatology Center

-- Michael Maricic, MD, Associate Professor of Clinical Medicine, University of Arizona, Chief of Rheumatology, Southern Arizona Veterans Administration Medical Center

Disclosure: Drs. Gluck and Maricic are consultants to Merck, Procter and Gamble, Aventis and Eli Lilly.

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<sup>1</sup> Neer RM, et al. *N Engl J Med.* 2001;344(19):1434-1441

ACR Hotline Editors: Arthur Kavanaugh, MD; Eric Matteson, MPH, MD

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