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PRESCRIBING ALERT®

Dear Healthcare Professional,

At *MPR* we strive to bring you important drug information in a concise and timely fashion. In keeping with this goal, we are pleased to bring you this PRESCRIBING ALERT announcing that FORTEO® (teriparatide [rDNA origin] injection), manufactured by Eli Lilly and Company, is now approved for the treatment of men and women with osteoporosis associated with sustained, systemic glucocorticoid therapy who are at high risk for fracture. In addition, FORTEO is indicated for the treatment of postmenopausal women with osteoporosis who are at high risk for fracture and to increase bone mass in men with primary or hypogonadal osteoporosis who are at high risk for fracture.[1]

Glucocorticoid therapy is the most common cause of secondary osteoporosis,[2] leading to bone loss and an increased risk for fracture. Data indicate that between 30% to 50% of individuals on sustained, systemic glucocorticoid therapy will develop significant bone loss, which can lead to an osteoporotic fracture.[3]

The efficacy and safety of FORTEO for the treatment of glucocorticoid-induced osteoporosis were evaluated in an 18-month, randomized, double-blind, active-controlled clinical trial of 428 men and women aged ≥21 years.[4] Patients receiving FORTEO had a significant increase in lumbar spine bone mineral density ($P<0.001$) from baseline at all time points.[4]

Important Safety Information

WARNING: POTENTIAL RISK OF OSTEOSARCOMA

In male and female rats, teriparatide caused an increase in the incidence of osteosarcoma (a malignant bone tumor) that was dependent on dose and treatment duration. The effect was observed at systemic exposures to teriparatide ranging from 3 to 60 times the exposure in humans given a 20-mcg dose. Because of the uncertain relevance of the rat osteosarcoma finding to humans, prescribe FORTEO® (teriparatide [rDNA origin] injection) only for patients for whom the potential benefits are considered to outweigh the potential risk. FORTEO should not be prescribed for patients who are at increased baseline risk for osteosarcoma (including those with Paget's disease of bone or unexplained elevations of alkaline phosphatase, pediatric and young adult patients with open epiphyses, or prior external beam or implant radiation therapy involving the skeleton).

CONTRAINDICATIONS

Hypersensitivity to teriparatide or to any of its excipients. Reactions have included angioedema and anaphylaxis.

WARNINGS AND PRECAUTIONS

The following categories of patients have increased baseline risk of osteosarcoma and therefore should not be treated with FORTEO: Paget's disease of bone, pediatric populations and young adults with open epiphyses, or prior external beam or implant radiation therapy.

Patients should be encouraged to enroll in the voluntary FORTEO Patient Registry, which is designed to collect information about any potential risk of osteosarcoma in patients who have taken FORTEO. Enrollment information can be obtained by calling 1-866-382-6813, or by visiting www.forteoregistry.rti.org.

(Important Safety Information for FORTEO continued on back)

Please see accompanying full Prescribing Information and Medication Guide for FORTEO.

Osteosarcoma occurs in about 4 out of every million older adults each year. Cases of bone tumor and osteosarcoma have been reported rarely in people taking FORTEO in the post-marketing period. The causality to FORTEO use is unclear.

Use of FORTEO for more than 2 years during a patient's lifetime is not recommended.

Patients with the following conditions also should not receive FORTEO: bone metastases or a history of skeletal malignancies, metabolic bone diseases other than osteoporosis, or hypercalcemic disorders.

FORTEO may increase serum calcium, urinary calcium, and serum uric acid.

Use with caution in patients with active or recent urolithiasis because of risk of exacerbation. If active urolithiasis or pre-existing hypercalciuria are suspected, measurement of urinary calcium excretion should be considered.

Transient orthostatic hypotension may occur with initial doses of FORTEO. In short-term clinical pharmacology studies, transient episodes of symptomatic orthostatic hypotension were observed in 5% of patients. FORTEO should be administered initially under circumstances where the patient can sit or lie down if symptoms of orthostatic hypotension occur.

Patients receiving digoxin should use FORTEO with caution because FORTEO may transiently increase serum calcium and hypercalcemia may predispose patients to digitalis toxicity.

FORTEO should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Based on animal studies, FORTEO may cause fetal harm.

It is not known whether teriparatide is excreted in human milk. Breastfeeding mothers should discontinue nursing or FORTEO, taking into account the importance of treatment to the mother.

ADVERSE REACTIONS

The most common adverse reactions in clinical trials include: arthralgia (10.1 FORTEO vs. 8.4 placebo), pain (21.3 FORTEO vs. 20.5 placebo), and nausea (8.5 FORTEO vs. 6.7 placebo). Other adverse reactions include: dizziness, leg cramps, joint aches, and injection site reactions.

INSTRUCTIONS FOR FORTEO USE

FORTEO is provided as a fixed-dose, prefilled delivery device that can be used for up to 28 days, including the first injection. The delivery device contains 28 daily doses of 20 mcg each. Do not transfer the contents of the delivery device into a syringe. The FORTEO Delivery Device should be stored under refrigeration at 36° to 46° F (2° to 8° C) at all times. Do not use FORTEO if it has been frozen.

Please see accompanying full Prescribing Information and Medication Guide for FORTEO.

More information about the use of FORTEO for the treatment of men and women with glucocorticoid-induced osteoporosis is available in the current edition of *MPR*.

Sincerely,

Grace L. McBride
Editorial Director
MPR Custom Programs

REFERENCES: 1. FORTEO [package insert]. Indianapolis, IN: Eli Lilly and Company; 2009. **2.** Mazziotti G, Angeli A, Bilezikian JP, et al. Glucocorticoid-induced osteoporosis: an update. *Endocrinol Metab.* 2006;17:144-149. **3.** Saag, KG. Glucocorticoid-induced osteoporosis. *Endocrinol Metab Clin N Am*. 2003;32:135-157. **4.** Saag KG, Shane E, Boonen S. et al. Teriparatide or alendronate in glucocorticoid-induced osteoporosis. *N Engl J Med.* 2007;357:2028-2039.

PRESCRIBING ALERT

FORTEO®

(teriparatide [rDNA origin] injection)

Company: Lilly USA, LLC. ℞

Pharmacologic class: Hormone (human parathyroid hormone, recombinant).

Indications: Treatment of postmenopausal women with osteoporosis at high risk for fracture. Increase bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture. Treatment of men and women with osteoporosis associated with sustained, systemic glucocorticoid therapy at high risk for fracture.

Adults: 20 mcg SC once daily into thigh or abdominal wall; may treat for up to 2 years in a patient's lifetime.

Children: Not indicated for use in pediatric or young adults with open epiphyses.

FORTEO delivery device

Pharmacology: Stimulates new bone formation on trabecular and cortical (periosteal and/or endosteal) bone surfaces by preferential stimulation of osteoblastic activity over osteoclastic activity. The anabolic effects of FORTEO manifest as an increase in skeletal mass, an increase in markers of bone formation and resorption, and an increase in bone strength.[1]

☑ FORTEO is now approved for use in glucocorticoid-induced osteoporosis (GIO)[1]

- FORTEO is indicated for the treatment of men and women with osteoporosis associated with sustained, systemic glucocorticoid therapy at high risk for fracture

☑ Sustained, systemic glucocorticoid use results in a suppression of bone formation

- It is thought that glucocorticoids primarily affect bone by inhibiting osteoblast activity, which leads to a decrease in bone formation[2,3]
  - Glucocorticoids decrease proliferation and differentiation of osteoblasts while enhancing apoptosis[3]
  - Apoptosis of osteocytes leads to a decrease in bone repair and an increase in bone fragility[3]
  - Early decrease in apoptosis of osteoclasts leads to a transient increase in bone resorption[2]

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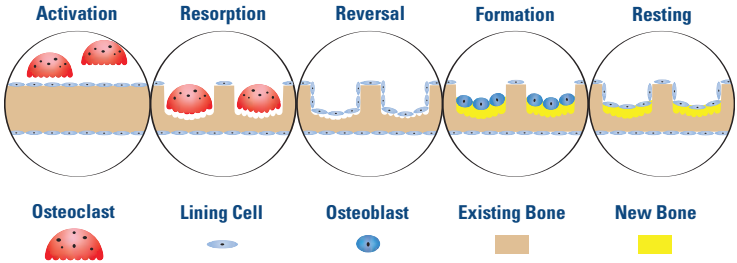
FORTEO® (teriparatide [rDNA origin] injection) strengthens bone by anabolic action[1]

- FORTEO increases the number and action of osteoblasts and stimulates new bone formation
- Resulting in:
  - Formation of new bone on cortical and trabecular surfaces
  - An increase in skeletal mass and bone strength

BONE REMODELING WITH FORTEO[1,4]

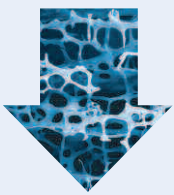


FORTEO may counteract the negative bone effects of glucocorticoids[5]

- In a study of patients with glucocorticoid-induced osteoporosis, FORTEO affected serum markers of bone turnover similar to those observed in postmenopausal women with osteoporosis not taking glucocorticoids

EFFECTS OF GLUCOCORTICOIDS AND FORTEO ON BONE

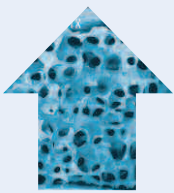
Sustained, systemic glucocorticoid use



DECREASES BONE FORMATION[3]

- Glucocorticoids impair the replication, differentiation, lifespan, and function of osteoblasts

FORTEO therapy



INCREASES BONE FORMATION[1,6,7]

- Increases the number and action of osteoblasts and osteoclasts
- Rebuilds bone

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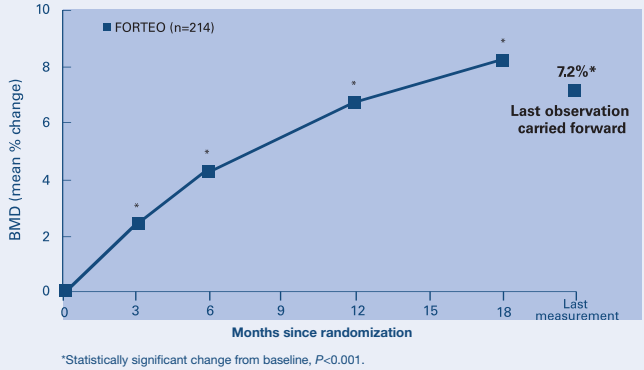
PRESCRIBING ALERT

- **FORTEO® (teriparatide [rDNA origin] injection) is indicated for the treatment of men and women with osteoporosis associated with sustained, systemic glucocorticoid therapy who are at high risk for fracture[1]**
  - Individuals at high risk for fracture include those who meet one of the following criteria (based on physician assessment):
    - Have a history of osteoporotic fracture, or
    - Have multiple risk factors for fracture, or
    - Failed or are intolerant to previous osteoporosis therapy
- **FORTEO significantly increases bone mineral density (BMD) from baseline at 18 months[5]**

CHANGES IN BONE MINERAL DENSITY[5]



*Statistically significant change from baseline, $P<0.001$.

- **FORTEO offers proven experience[1,8]**
  - More than 3.5 million prescriptions worldwide
  - Over 6 years on the market
- **GIO is primarily a disease of reduced bone formation, and therefore, anabolic therapy with FORTEO is an approved treatment strategy[1,2]**
- **In patients with GIO treated with FORTEO for 18 months, the following results were observed[5]:**
  - Lumbar spine and total hip BMD increased significantly

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REFERENCES: 1. FORTEO [package insert]. Indianapolis, IN: Eli Lilly and Company; 2009. **2.** Weinstein RS. Glucocorticoid-induced osteoporosis. In: Rosen CJ, ed. *Primer on the Metabolic Bone Diseases and Disorders of Mineral Metabolism.* 7th ed. Washington, DC: ASBMR; 2008;267-272. **3.** Canalis E, Mazziotti G, Giustina A, Bilezikian JP. Glucocorticoid-induced osteoporosis: pathophysiology and therapy. *Osteoporos Int.* 2007; 18:1319-1328. **4.** Lindsay R, Cosman F. Osteoporosis. In: Fauci AS, Braunwald E, Kasper DL, et al. *Harrison's Principles of Internal Medicine,* 17th ed. USA. 2008;2397-2407. **5.** Saag KG, Shane E, Boonen S, et al. Teriparatide or alendronate in glucocorticoid-induced osteoporosis. *N Engl J Med.* 2007;357:2028-2039. **6.** National Osteoporosis Foundation. Medications to prevent and treat osteoporosis. Available at: http://www.nof.org/patientinfo/medications.htm. Accessed September 14, 2009. **7.** National Osteoporosis Foundation. Clinician's guide to prevention and treatment of osteoporosis. 2008. Available at: http://www.nof.org/professionals/resources.htm. Accessed September 14, 2009. **8.** Data on file, Lilly Research Laboratories (FOR20080317A).