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## Appendix 4. FORTEO<sup>®</sup> (teriparatide rDNA origin) injection Highlighted Information for Prescribers

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### Potential Risk of Osteosarcoma and the Voluntary FORTEO Patient Registry

This information is being provided to prescribers of FORTEO as part of the Risk Evaluation and Mitigation Strategy (REMS) plan for FORTEO. REMS plans have been required for certain drugs with serious risks since 2008 by the U.S. Food and Drug Administration to ensure that the benefits of the drug outweigh the risks of the drug.

The purpose of this information is to inform prescribers of FORTEO about the following:

- Proper patient selection and 2 years maximum lifetime duration of treatment
- Potential risk of osteosarcoma
- Voluntary FORTEO Patient Registry

*Refer to the Full Prescribing Information for further product information.*

### **INDICATIONS AND USAGE**

FORTEO is indicated:

- for the treatment of postmenopausal women with osteoporosis at high risk for fracture
- to increase bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture
- for the treatment of men and women with glucocorticoid-induced osteoporosis at high risk for fracture

These patients include women and men with a history of osteoporotic fracture, or who have multiple risk factors for fracture, or who have failed or are intolerant of previous osteoporosis therapy, based upon physician assessment.

### **TREATMENT DURATION**

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

### **POTENTIAL RISK OF OSTEOSARCOMA**

FORTEO labeling contains a boxed warning describing the 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, teriparatide should be prescribed only to 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
  - Prior external beam or implant radiation therapy involving the skeleton

Additional warnings in the label state that patients with the following conditions should not receive FORTEO:

- Bone metastases or a history of skeletal malignancies
- Metabolic bone diseases other than osteoporosis
- Pre-existing hypercalcemia

#### **POSTMARKETING EXPERIENCE: OSTEOSARCOMA**

Cases of bone tumor and osteosarcoma have been reported rarely in the postmarketing period. The causality to FORTEO use is unclear.

Osteosarcoma is a serious but rare cancer. The incidence in the general population over the age of 60 in the United States is approximately 4 per million per year. The incidence of osteosarcoma in patients taking FORTEO is unknown. The first report of osteosarcoma in a patient treated with FORTEO has been published (*J Bone Miner Res.* 2007;22:334).

#### **VOLUNTARY FORTEO PATIENT REGISTRY**

A voluntary FORTEO Patient Registry has been established to collect information about any potential risk of osteosarcoma in patients who have taken FORTEO. Prescribers of FORTEO should encourage patients to enroll in the registry. The time burden for the patient is minimal (3-5 minutes). Beyond encouraging patients to participate, no further action is necessary for prescribers of FORTEO.

The voluntary FORTEO Patient Registry is being conducted by RTI International (RTI), a nonprofit research organization. All information collected as part of the registry will be kept strictly confidential by RTI, and information that can identify patients will not be shared with Eli Lilly and Company (the sponsor of this registry) or with anyone outside of the research team.

Targeted patient information including name, address, date of birth, and last 4 digits of social security number will be provided by patients one time only for entry into the registry. Annually for 12 years, this information will be linked by a secure process to participating state cancer registry databases. Currently, state cancer registries capture newly diagnosed cases of cancer.

Data from this linkage will be analyzed along with information from other studies to help evaluate whether FORTEO patients have an increased risk for developing osteosarcoma. The

results will be published after the last linkage. Patients who do not wish to participate in the registry can still receive FORTEO treatment.

Patient participation is voluntary and involves a three-step process:

- Step 1: Patient completes a short pre-enrollment form and mails to RTI.
- Step 2: After receiving the pre-enrollment form, RTI mails the patient an informed consent form, a short registration form, and a modest reimbursement for the patient's time in completing the forms.
- Step 3: Patient completes and mails the informed consent and registration back to RTI. Patient involvement is completed.

Pre-enrollment forms are available to patients in each filled FORTEO prescription and may also be obtained from FORTEO prescribers. Healthcare providers may obtain further information about the registry or request pre-enrollment forms by calling the RTI registry hotline at 1-866-382-6813 or visiting [www.FORTEORegistry.rti.org](http://www.FORTEORegistry.rti.org).

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CHRISTINE P NGUYEN  
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