Prolia™, Xgeva® (denosumab) – New Warning

- On January 31, 2017, the FDA approved a new update to the *Warnings and Precautions* section of the Prolia (denosumab) and Xgeva (denosumab) drug labels regarding the risk of multiple vertebral fractures following discontinuation of denosumab treatment.

- Per Amgen, the same safety update applies to Xgeva; however, an updated drug label is not yet available.

- Prolia is indicated for the following:

    - Treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy
    - Treatment to increase bone mass in men with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy
    - Treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for non-metastatic prostate cancer
    - Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer

- Xgeva is indicated for the following:

    - Prevention of skeletal-related events in patients with bone metastases from solid tumors
        - Xgeva is not indicated for the prevention of skeletal-related events in patients with multiple myeloma
    - Treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity
    - Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy

- Following discontinuation of Prolia treatment, fracture risk increases, including the risk of multiple vertebral fractures. Cessation of Prolia treatment results in markers of bone resorption increasing above pretreatment values then returning to pretreatment values 24 months after the last dose of Prolia. In addition, bone mineral density returns to pretreatment values within 18 months after the last injection.

    - New vertebral fractures occurred as early as 7 months (on average 19 months) after the last dose of Prolia. Prior vertebral fracture was a predictor of multiple vertebral fractures after Prolia discontinuation.
    - An individual's benefit/risk should be evaluated before initiating treatment with Prolia.
    - If Prolia treatment is discontinued, transitioning to an alternative antiresorptive therapy should be considered.

- Similar updates were made to the Prolia Medication Guide.

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- An additional update to the Prolia drug label includes the removal of information regarding Amgen's Pregnancy Surveillance Program from the Pregnancy subsection of the *Use in Specific Populations* section.