Evenity™ (romosozumab-aqqg) – New drug approval

- On April 9, 2019, the FDA announced the approval of Amgen's Evenity (romosozumab-aqqg), for the treatment of osteoporosis in postmenopausal women 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.
    - The anabolic effect of Evenity wanes after 12 monthly doses of therapy. Therefore, the duration of Evenity use should be limited to 12 monthly doses. If osteoporosis therapy remains warranted, continued therapy with an anti-resorptive agent should be considered.
- More than 10 million people in the U.S. have osteoporosis, which is most common in women who have gone through menopause. Osteoporosis is responsible for an estimated two million fractures per year. After the first fracture, a woman is five times more likely to suffer another fracture within a year.
- Evenity is a first-in-class humanized monoclonal antibody that inhibits the action of sclerostin, a regulatory factor in bone metabolism. Evenity increases bone formation and, to a lesser extent, decreases bone resorption.
- The efficacy of Evenity was established in two double-blind studies involving more than 11,000 women with postmenopausal osteoporosis. In study 1, women were randomized to receive Evenity (n = 3,589) or placebo (n = 3,591) for 12 months. After the 12-month treatment period, women in both arms transitioned to open-label anti-resorptive therapy (Prolia® [denosumab]) for 12 months. The co-primary efficacy endpoints were new vertebral fracture at month 12 and month 24. In study 2, women were randomized to receive Evenity (n = 2046) or oral alendronate (n = 2047) for 12 months. After the 12-month treatment period, women in both arms transitioned to open-label alendronate. The co-primary efficacy endpoints were the incidence of vertebral fracture at 24 months and time to the first clinical fracture.
    - In study 1, new vertebral fracture occurred in 0.5% and 1.8% of patients receiving Evenity and placebo, respectively ($p < 0.001$). The absolute risk reduction was 1.3% (95% CI: 0.8, 1.8) and the relative risk reduction was 73% (95% CI: 53, 84). The significant reduction in fracture risk persisted through the second year (0.6% vs. 2.5% with Evenity followed by Prolia vs. placebo followed by Prolia, respectively).
    - In study 2, new vertebral fracture through month 24 occurred in 4.1% and 8.0% of patients receiving Evenity followed by alendronate vs. alendronate alone, respectively ($p < 0.001$). The absolute risk reduction was 4.0% (95% CI: 2.5, 5.6) and the relative risk reduction was 50% (95% CI: 34, 62). In addition, 9.7% and 13.0% of patients had a clinical fracture through the primary analysis period with Evenity followed by alendronate vs. alendronate alone, respectively (Hazard Ratio 0.73; 95% CI: 0.61, 0.88; $p < 0.001$).
- Evenity carries a boxed warning for potential risk of myocardial infarction, stroke, and cardiovascular death.
    - This approval comes with a post-marketing requirement from the FDA to assess the cardiovascular safety of Evenity in postmenopausal osteoporosis women.
- Evenity is contraindicated in patients with hypocalcemia or a history of systemic hypersensitivity to romosozumab or to any component of the product formulation.
- Additional warnings and precautions of Evenity include hypersensitivity reactions, hypocalcemia, osteonecrosis of the jaw, and atypical subtrochanteric and diaphyseal femoral fractures.

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- The most common adverse reactions (≥ 5%) with Evenity use were arthralgia and headache.
- The recommended dose of Evenity is 210 mg administered once every month subcutaneously in the abdomen, thigh or upper arm.
    - Evenity should be administered by a healthcare provider
    - Two separate syringes (and two separate subcutaneous injections) are needed to administer the total dose of 210 mg of Evenity.
    - Patients should be adequately supplemented with calcium and vitamin D during treatment with Evenity.
- Amgen plans to launch Evenity in approximately one week. Evenity will be available as a 105 mg/1.17 mL solution in a single-use prefilled syringe.