

FOR THE TREATMENT OF POSTMENOPAUSAL WOMEN WITH  
OSTEOPOROSIS AT HIGH RISK FOR FRACTURE

Every patient has a different starting point

**MEET HER THERE**

Start by assessing her fracture risk

For your patients with a  
**prior fracture or very low T-score**  
(eg, less than -3.0) with other risk  
factors, start with the  
sequence of **EVENTITY®**  
followed by **Prolia®**  
to help build and  
protect her bone.<sup>1,2,3</sup>

For your patients with  
**no prior fracture and low T-score**  
(less than or equal to -2.5)  
with other risk factors,  
start with **Prolia®**  
to help strengthen  
her bone.<sup>3,4,5</sup>



Artist rendering of bone imagery for illustrative purposes only.



**INDICATION:**

EVENTITY® is indicated 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 EVENTITY® wanes after 12 monthly doses of therapy. Therefore, the duration of EVENTITY® use should be limited to 12 monthly doses. If osteoporosis therapy remains warranted, continued therapy with an antiresorptive agent should be considered.

**IMPORTANT SAFETY INFORMATION**

**POTENTIAL RISK OF MYOCARDIAL INFARCTION, STROKE, AND CARDIOVASCULAR DEATH**

EVENTITY® may increase the risk of myocardial infarction, stroke and cardiovascular death. EVENTITY® should not be initiated in patients who have had a myocardial infarction or stroke within the preceding year. Consider whether the benefits outweigh the risks in patients with other cardiovascular risk factors. Monitor for signs and symptoms of myocardial infarction and stroke and instruct patients to seek prompt medical attention if symptoms occur. If a patient experiences a myocardial infarction or stroke during therapy, EVENTITY® should be discontinued.

Please see additional EVENTITY® Important Safety Information on page 3.



**INDICATION:**

Prolia® is indicated for the 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. In postmenopausal women with osteoporosis, Prolia® reduces the incidence of vertebral, nonvertebral, and hip fractures.

**IMPORTANT SAFETY INFORMATION**

**Contraindications:** Prolia® is contraindicated in patients with hypocalcemia. Pre-existing hypocalcemia must be corrected prior to initiating Prolia®. Prolia® is contraindicated in women who are pregnant and may cause fetal harm. In women of reproductive potential, pregnancy testing should be performed prior to initiating treatment with Prolia®. Prolia® is contraindicated in patients with a history of systemic hypersensitivity to any component of the product. Reactions have included anaphylaxis, facial swelling and urticaria.

Please see additional Prolia® Important Safety Information on pages 4 and 5.

# 2020 AACE/ACE stratification criteria for fracture risk and treatment recommendations<sup>3</sup>

## **VERY HIGH RISK FOR FRACTURE** (At least 1 of these criteria qualifies as very high risk)

- Had recent fracture (within past 12 months)
- Had fracture while on approved therapy for osteoporosis
- Had fractures while on drugs that may cause skeletal harm
- Experienced multiple fractures
- Very low T-score (less than -3.0)
- High risk for falls or history of injurious falls
- Very high fracture probability by FRAX® (major osteoporotic fracture > 30%, > 4.5% hip)

**Recommended initial therapy\*:** abaloparatide, **denosumab**, **romosozumab-aqqg**, teriparatide, zoledronate

**Alternative therapy:** alendronate and risedronate

## **HIGH RISK FOR FRACTURE** (At least 1 of these criteria qualifies as high risk)

- Osteopenia or low bone mass and a history of fragility fracture of the hip or spine
- T-score of -2.5 or lower in the lumbar spine, femoral neck, total hip, or 33% (1/3) radius
- T-score of -1.0 to -2.5 and increased fracture risk using fracture risk assessment tool FRAX® (10-year probability of any major osteoporotic fracture ≥ 20%; hip fracture ≥ 3%)

**Recommended initial therapy:** alendronate, **denosumab**, risedronate, zoledronate

**Alternative therapy:** ibandronate or raloxifene<sup>†</sup>

\*Therapies listed are also recommended for patients unable to use oral therapies.

<sup>†</sup>Patients requiring medication with spine-specific efficacy.

AACE = American Association of Clinical Endocrinologists; ACE = American College of Endocrinology; FRAX® = fracture risk assessment tool.

FRAX® is a registered trademark of Professor JA Kanis, University of Sheffield.

Please see EVENITY® (romosozumab-aqqg) Important Safety Information on page 3.

Please see Prolia® (denosumab) Important Safety Information on pages 4 and 5.

## **EVENTITY® (romosozumab-aqqg) IMPORTANT SAFETY INFORMATION**

### **POTENTIAL RISK OF MYOCARDIAL INFARCTION, STROKE, AND CARDIOVASCULAR DEATH**

EVENTITY® may increase the risk of myocardial infarction, stroke and cardiovascular death. EVENTITY® should not be initiated in patients who have had a myocardial infarction or stroke within the preceding year. Consider whether the benefits outweigh the risks in patients with other cardiovascular risk factors. Monitor for signs and symptoms of myocardial infarction and stroke and instruct patients to seek prompt medical attention if symptoms occur. If a patient experiences a myocardial infarction or stroke during therapy, EVENTITY® should be discontinued.

In a randomized controlled trial in postmenopausal women, there was a higher rate of major adverse cardiac events (MACE), a composite endpoint of cardiovascular death, nonfatal myocardial infarction and nonfatal stroke, in patients treated with EVENTITY® compared to those treated with alendronate.

**Contraindications:** EVENTITY® is contraindicated in patients with hypocalcemia. Pre-existing hypocalcemia must be corrected prior to initiating therapy with EVENTITY®. EVENTITY® is contraindicated in patients with a history of systemic hypersensitivity to romosozumab or to any component of the product formulation. Reactions have included angioedema, erythema multiforme, and urticaria.

**Hypersensitivity:** Hypersensitivity reactions, including angioedema, erythema multiforme, dermatitis, rash, and urticaria have occurred in EVENTITY®-treated patients. If an anaphylactic or other clinically significant allergic reaction occurs, initiate appropriate therapy and discontinue further use of EVENTITY®.

**Hypocalcemia:** Hypocalcemia has occurred in patients receiving EVENTITY®. Correct hypocalcemia prior to initiating EVENTITY®. Monitor patients for signs and symptoms of hypocalcemia, particularly in patients with severe renal impairment or receiving dialysis. Adequately supplement patients with calcium and vitamin D while on EVENTITY®.

**Osteonecrosis of the Jaw (ONJ):** ONJ, which can occur spontaneously, is generally associated with tooth extraction and/or local infection with delayed healing, and has been reported in patients receiving EVENTITY®. A routine oral exam should be performed by the prescriber prior to initiation of EVENTITY®. Concomitant administration of drugs associated with ONJ (chemotherapy, bisphosphonates, denosumab, angiogenesis inhibitors, and corticosteroids) may increase the risk of developing ONJ. Other risk factors for ONJ include cancer, radiotherapy, poor oral hygiene, pre-existing dental disease or infection, anemia, and coagulopathy. For patients requiring invasive dental procedures, clinical judgment should guide the management plan of each patient. Patients who are suspected of having or who develop ONJ should receive care by a dentist or an oral surgeon. In these patients, dental surgery to treat ONJ may exacerbate the condition. Discontinuation of EVENTITY® should be considered based on benefit-risk assessment.

**Atypical Femoral Fractures:** Atypical low-energy or low trauma fractures of the femoral shaft have been reported in patients receiving EVENTITY®. Causality has not been established as these fractures also occur in osteoporotic patients who have not been treated.

During EVENTITY® treatment, patients should be advised to report new or unusual thigh, hip, or groin pain. Any patient who presents with thigh or groin pain should be evaluated to rule out an incomplete femur fracture. Interruption of EVENTITY® therapy should be considered based on benefit-risk assessment.

**Adverse Reactions:** The most common adverse reactions ( $\geq 5\%$ ) reported with EVENTITY® were arthralgia and headache.

EVENTITY® is a humanized monoclonal antibody. As with all therapeutic proteins, there is potential for immunogenicity.

**Please see EVENTITY® full Prescribing Information, including Medication Guide.**

## **PROLIA® (denosumab) IMPORTANT SAFETY INFORMATION**

**Contraindications:** Prolia® is contraindicated in patients with hypocalcemia. Pre-existing hypocalcemia must be corrected prior to initiating Prolia®. Prolia® is contraindicated in women who are pregnant and may cause fetal harm. In women of reproductive potential, pregnancy testing should be performed prior to initiating treatment with Prolia®. Prolia® is contraindicated in patients with a history of systemic hypersensitivity to any component of the product. Reactions have included anaphylaxis, facial swelling and urticaria.

**Same Active Ingredient:** Prolia® contains the same active ingredient (denosumab) found in XGEVA®. Patients receiving Prolia® should not receive XGEVA®.

**Hypersensitivity:** Clinically significant hypersensitivity including anaphylaxis has been reported with Prolia®. Symptoms have included hypotension, dyspnea, throat tightness, facial and upper airway edema, pruritus and urticaria. If an anaphylactic or other clinically significant allergic reaction occurs, initiate appropriate therapy and discontinue further use of Prolia®.

**Hypocalcemia:** Hypocalcemia may worsen with the use of Prolia®, especially in patients with severe renal impairment. In patients predisposed to hypocalcemia and disturbances of mineral metabolism, including treatment with other calcium-lowering drugs, clinical monitoring of calcium and mineral levels is highly recommended within 14 days of Prolia® injection. Concomitant use of calcimimetic drugs may worsen hypocalcemia risk and serum calcium should be closely monitored. Adequately supplement all patients with calcium and vitamin D.

**Osteonecrosis of the Jaw (ONJ):** ONJ, which can occur spontaneously, is generally associated with tooth extraction and/or local infection with delayed healing, and has been reported in patients receiving Prolia®. An oral exam should be performed by the prescriber prior to initiation of Prolia®. A dental examination with appropriate preventive dentistry is recommended prior to treatment in patients with risk factors for ONJ such as invasive dental procedures, diagnosis of cancer, concomitant therapies (e.g. chemotherapy, corticosteroids, angiogenesis inhibitors), poor oral hygiene, and co-morbid disorders. Good oral hygiene practices should be maintained during treatment with Prolia®. The risk of ONJ may increase with duration of exposure to Prolia®.

For patients requiring invasive dental procedures, clinical judgment should guide the management plan of each patient. Patients who are suspected of having or who develop ONJ should receive care by a dentist or an oral surgeon. Extensive dental surgery to treat ONJ may exacerbate the condition. Discontinuation of Prolia® should be considered based on individual benefit-risk assessment.

**Atypical Femoral Fractures:** Atypical low-energy, or low trauma fractures of the shaft have been reported in patients receiving Prolia®. Causality has not been established as these fractures also occur in osteoporotic patients who have not been treated with antiresorptive agents.

During Prolia® treatment, patients should be advised to report new or unusual thigh, hip, or groin pain. Any patient who presents with thigh or groin pain should be evaluated to rule out an incomplete femur fracture. Interruption of Prolia® therapy should be considered, pending a risk/benefit assessment, on an individual basis.

**Multiple Vertebral Fractures (MVF) Following Discontinuation of Prolia® Treatment:** Following discontinuation of Prolia® treatment, fracture risk increases, including the risk of multiple vertebral fractures. 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. Evaluate an individual's benefit/risk before initiating treatment with Prolia®. If Prolia® treatment is discontinued, patients should be transitioned to an alternative antiresorptive therapy.

## **PROLIA® (denosumab) IMPORTANT SAFETY INFORMATION (cont.)**

**Serious Infections:** In a clinical trial (N = 7808), serious infections leading to hospitalization were reported more frequently in the Prolia® group than in the placebo group. Serious skin infections, as well as infections of the abdomen, urinary tract and ear, were more frequent in patients treated with Prolia®.

Endocarditis was also reported more frequently in Prolia®-treated patients. The incidence of opportunistic infections and the overall incidence of infections were similar between the treatment groups. Advise patients to seek prompt medical attention if they develop signs or symptoms of severe infection, including cellulitis.

Patients on concomitant immunosuppressant agents or with impaired immune systems may be at increased risk for serious infections. In patients who develop serious infections while on Prolia®, prescribers should assess the need for continued Prolia® therapy.

**Dermatologic Adverse Reactions:** Epidermal and dermal adverse events such as dermatitis, eczema and rashes occurred at a significantly higher rate with Prolia® compared to placebo. Most of these events were not specific to the injection site. Consider discontinuing Prolia® if severe symptoms develop.

**Musculoskeletal Pain:** Severe and occasionally incapacitating bone, joint, and/or muscle pain has been reported in patients taking Prolia®. Consider discontinuing use if severe symptoms develop.

**Suppression of Bone Turnover:** Prolia® resulted in significant suppression of bone remodeling as evidenced by markers of bone turnover and bone histomorphometry. The significance of these findings and the effect of long-term treatment are unknown. Monitor patients for consequences, including ONJ, atypical fractures, and delayed fracture healing.

**Adverse Reactions:** The most common adverse reactions (>5% and more common than placebo) are back pain, pain in extremity, musculoskeletal pain, hypercholesterolemia, and cystitis. Pancreatitis has been reported with Prolia®.

The overall incidence of new malignancies was 4.3% in the placebo group and 4.8% in the Prolia® group. A causal relationship to drug exposure has not been established. Denosumab is a human monoclonal antibody. As with all therapeutic proteins, there is potential for immunogenicity.

**Please see Prolia® full Prescribing Information, including Medication Guide.**

## FOR THE TREATMENT OF POSTMENOPAUSAL WOMEN WITH OSTEOPOROSIS AT HIGH RISK FOR FRACTURE



### Risk factors for fracture may include:<sup>3,6</sup>



Prior fragility fracture



Low BMD  
(T-score  $\leq$  -2.5)



Age  
 $\geq$  65 years



Low body weight



Long-term glucocorticoid use



Excessive alcohol intake  
( $>$  3 drinks/day)



Cigarette smoking



Immobilization



Parental history of hip fracture



Risk of falling



Rheumatoid arthritis



Diabetes

BMD = bone mineral density.

Please see EVENITY® (romosozumab-aqqg) Important Safety Information on page 3.

Please see Prolia® (denosumab) Important Safety Information on pages 4 and 5.

**References:** 1. EVENITY® (romosozumab-aqqg) prescribing information, Amgen. 2. Lewiecki EM, Dinavahi RV, Lazaretti-Castro M, et al. One year of romosozumab followed by two years of denosumab maintains fracture risk reductions: results of the FRAME extension study. *J Bone Miner Res*. 2019;34:419-428. 3. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology Clinical Practice Guidelines for the Diagnosis and Treatment of Postmenopausal Osteoporosis-2020. *Endoc Pract*. 2020;26 (suppl 1):1-46. 4. Prolia® (denosumab) prescribing information, Amgen. 5. Keaveny TM, McClung MR, Genant HK, et al. Femoral and vertebral strength improvements in postmenopausal women with osteoporosis treated with denosumab. *J Bone Miner Res*. 2014;29:158-165. 6. National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. Washington, DC: National Osteoporosis Foundation; 2014.



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