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Help Build Bones with an Osteoporosis Treatment Option

Announcer: You're listening to ReachMD.

This medical industry feature, titled "**Help Build Bones with an Osteoporosis Treatment Option"** is sponsored by Amgen. This program is intended for members of the healthcare community.

Here's your host, Dr. Jennifer Caudle.

Dr. Caudle: Half of all US women over age 50 will have an osteoporosis-related fracture in their lifetime.[1] And in the year after her first fracture, a postmenopausal woman with osteoporosis is five times more likely to suffer another.[2] Several treatments are available to reduce fracture risk[3] and today we will discuss an osteoporosis treatment option called EVENITY®, also known as romosozumab, which was approved by the FDA.[4]

Announcer: EVENITY® 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.

EVENITY® has a limitation of use. 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 antiresorptive agent should be considered.[4]

The boxed warning for EVENITY® states that EVENITY® may increase the risk of myocardial infarction, stroke and cardiovascular death. EVENITY® 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, EVENITY® should be discontinued.

Dr. Caudle: Welcome to ReachMD. I'm your host Dr. Jennifer Caudle and joining me to discuss this treatment option for postmenopausal osteoporosis is Dr. Michael McClung, founding director of the Oregon Osteoporosis Center and Adjunct Professor of Medicine at the Oregon Health & Science University, and Dr. Robin Dore, Clinical Professor of Medicine at UCLA's David Geffen School of Medicine. Drs. McClung and Dore, thank you for joining me today.

Dr. McClung: Yes, it's a pleasure to be here. Thank you.

Dr. Dore: Thank you very much. Glad to be here, as well.

Dr. Caudle: So, to start us off, Dr. McClung, what can you tell us about EVENITY®?

Dr. McClung: Well, EVENITY® is a humanized monoclonal antibody against a protein called sclerostin, an important inhibitor of bone formation.[4] The mechanism of action of EVENITY® on skeletal health is unique.[4-6] EVENITY® increases bone formation while simultaneously decreasing bone resorption to a lesser extent.[4] EVENITY® was approved in April of this year for the treatment of women with postmenopausal osteoporosis at high risk of fracture.[4]

Dr. Caudle: There were two pivotal phase 3 trials that helped bring EVENITY® to market.[4] Can you give me a quick overview of these?

Dr. Dore: Yes, the FRAME study was EVENITY® followed by denosumab versus placebo followed by denosumab, and in the study there was a significant relative risk reduction in new vertebral fracture risk at 12 months of 73%. There were also large increases in bone density compared to placebo. The difference in lumbar spine bone density was 12.7% at 12 months, the total hip 5.8% at 12 months, and the femoral neck 5.2% at 12 months. The incidence of nonvertebral fractures was not statistically significantly different when comparing EVENITY®-treated women to the placebo-treated women.[4,7]

The other study was the ARCH trial, and this was an event-driven, head-to-head trial of EVENITY® followed by alendronate versus alendronate alone. This included patients with postmenopausal osteoporosis at high risk for fracture. There was a significant relative risk reduction in new vertebral fractures of 50% at 24 months, and nonvertebral fracture risk reduction of 19% at the primary analysis. Rapid increases in bone density were seen at month 12 compared to alendronate.[4,8]

Dr. Caudle: Now that we talked about efficacy, what can you tell our listeners about the safety of EVENITY® in these clinical trials?

Dr. McClung: The data from the trials demonstrated a generally favorable benefit-risk profile over the duration of the clinical studies of EVENITY® followed by an antiresorptive. The most common adverse reactions observed with EVENITY® occurring at a rate of 5% or more were arthralgia and headache. There was a prespecified plan to adjudicate every serious adverse event related to cardiovascular outcomes. In the FRAME study compared to placebo, there was no difference in the frequency of events between placebo and EVENITY®.[4] However, in the ARCH trial, compared to alendronate, there was a numeric imbalance with more serious cardiovascular events with EVENITY® compared to alendronate.[4] In the adjudication process, the serious cardiovascular events were refined into a category called MACE, or major adverse cardiac events, and when that endpoint was evaluated, there was a statistically significantly greater increase in the incidence of MACE events in the EVENITY® arm, 2%, compared to the alendronate arm, 1.1%, resulting in a hazard ratio over the first 12 months of therapy of 1.87 for EVENITY® compared to alendronate.[4] Attempts to explain the disparity between the difference in MACE events in the ARCH study compared to alendronate with no signal being seen in the FRAME study compared to placebo has been unclear, but recognizing that the signal existed led to the inclusion of the boxed warning for EVENITY®.

Dr. Caudle: For those of you who are just joining us, this is ReachMD.

I'm your host Dr. Jennifer Caudle and today, I'm speaking with Drs. McClung and Dore about the approved postmenopausal osteoporosis therapy called EVENITY®.[4] We spoke a bit earlier about the clinical studies and the effect of EVENITY® on vertebral fracture risk reduction and bone mineral density gains in postmenopausal women at high risk for fracture. But now let's shift gears a bit and talk about its use in clinical practice.

So, Dr. Dore, what other important information do healthcare providers need to know about treating a patient with EVENITY®?

Dr. Dore: It's important to understand that it is a monthly, subcutaneous injection that is given for a total of 12 months, and there's limited use up to those 12 monthly doses.[4] The patients have to make certain that they are getting adequate amounts of calcium and vitamin D when they're taking this treatment.[4] It is important to consider following EVENITY® with an antiresorptive drug to maintain or improve the gains in bone density.[4]

Dr. Caudle: Okay, and thank you for that, and Dr. McClung, many women with PMO may have already been treated with bisphosphonates. Are they candidates for EVENITY®?

Dr. McClung: Yes. That's a very important and practical clinical question. After several years of therapy with bisphosphonates, many patients remain at high risk of fracture and those would be appropriate candidates to consider EVENITY®.[4] Studies have been done demonstrating that women who have previously received bisphosphonates, when transitioned to EVENITY®, have an additional gain in bone mineral density in both the hip and the spine.

Dr. Caudle: Wonderful. So, let's talk about which patients could benefit from EVENITY®. Dr. Dore, who is an appropriate candidate for EVENITY®?

Dr. Dore: Well, Dr. McClung has already mentioned EVENITY® is indicated for postmenopausal women with osteoporosis at high risk for fracture,[4] so this is the patient that we are going to be looking at. And then someone who we feel is an appropriate candidate for anabolic therapy, who hasn't had an MI or stroke during the last year.[4]

Dr. Caudle: Dr. McClung, what are your thoughts?

Dr. McClung: Uh, to second Dr. Dore's comments, in the case of thinking about EVENITY® and the patient for which it was appropriate,

it is appropriate to consider the benefit-risk ratio. So, as Dr. Dore outlined, identifying patients at high risk of fracture, which is quite straightforward to do, is the first step, and then we would avoid EVENITY® therapy in patients who had a stroke or MI within the year before their evaluation.[4] Another question I'm frequently asked about EVENITY® is whether it is effective in men, EVENITY® is not approved for the treatment of osteoporosis in men.

Dr. Caudle: Okay, and doctors, before we close our discussion today, are there any final thoughts you'd like to share for our audience? Dr. Dore, why don't we start with you first.

Dr. Dore: Well, from my point of view, EVENITY® is very exciting because it has a unique mechanism of action,[4-6] as Dr. McClung discussed at the beginning. It has a dual effect, increasing bone formation and, to a lesser extent, decreasing bone resorption.[4] And in the clinical trials, EVENITY® was shown to reduce both fracture risk and to increase bone density.[4]

Dr. Caudle: Thanks, Dr. Dore. Dr. McClung, any additional takeaways?

Dr. McClung: Only to reiterate that EVENITY® is a very good option for women at high risk of fracture.[4] And I think EVENITY® is a very important addition to our menu of treatment options.

Dr. Caudle: Excellent. And, Dr. Dore, any additional takeaways?

Dr. Dore: No, I'd just like to second his thought. From my point of view, it's very exciting to have medication that has a unique mechanism of action, and there's so many patients who could benefit from anabolic therapy. It's really nice to have another anabolic therapy available for our patients.

Announcer:

Important Safety Information

POTENTIAL RISK OF MYOCARDIAL INFARCTION, STROKE, AND CARDIOVASCULAR DEATH

EVENITY® may increase the risk of myocardial infarction, stroke and cardiovascular death. EVENITY® 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 EVENITY® should be discontinued.

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

Contraindications: EVENITY® is contraindicated in patients with hypocalcemia. Pre-existing hypocalcemia must be corrected prior to initiating therapy with EVENITY®. EVENITY® 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 EVENITY®-treated patients. If an anaphylactic or other clinically significant allergic reaction occurs, initiate appropriate therapy and discontinue further use of EVENITY®.

Hypocalcemia: Hypocalcemia has occurred in patients receiving EVENITY®. Correct hypocalcemia prior to initiating EVENITY®. 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 EVENITY®.

Osteonecrosis of the Jaw (or 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 EVENITY®. A routine oral exam should be performed by the prescriber prior to initiation of EVENITY®. 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 EVENITY® 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 EVENITY®. Causality has not been established as these fractures also occur in osteoporotic patients who have not been treated.

During EVENITY® 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 EVENITY® therapy should be considered based on benefit-risk assessment.

Adverse Reactions: The most common adverse reactions (≥ 5%) reported with EVENITY® were arthralgia and headache.

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

Please see EVENITY® full Prescribing Information including Boxed Warning and Medication Guide at www.evenityhcp.com.

Dr. Caudle: So, with that, I'd really like to thank you, Drs. McClung and Dore, for breaking down all of that information for us on EVENITY®. It was wonderful speaking with you both today.

Dr. McClung: Yes, well, thank you for this opportunity.

Dr. Dore: Thank you very much for including us in the discussion.

Announcer: This program was sponsored by Amgen. If you missed any part of this discussion, visit Reachmd.com/**Osteoporosis.** This is ReachMD. Be part of the knowledge

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