From: [Managed Healthcare Executive; edigest…]
To: [Insert Customer Email]
Cc:

A study of EVENITY® (romosozumab-aqqg)

Yesterday at 6:25 PM

For the treatment of postmenopausal women with osteoporosis at high risk for fracture.

EVENITY® for 12 months followed by alendronate provided superior vertebral and nonvertebral fracture risk reduction vs alendronate alone[1]

EVENITY® (romosozumab-aqqg) injection 105 mg/1.17 mL

INDICATION

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.

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.

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.

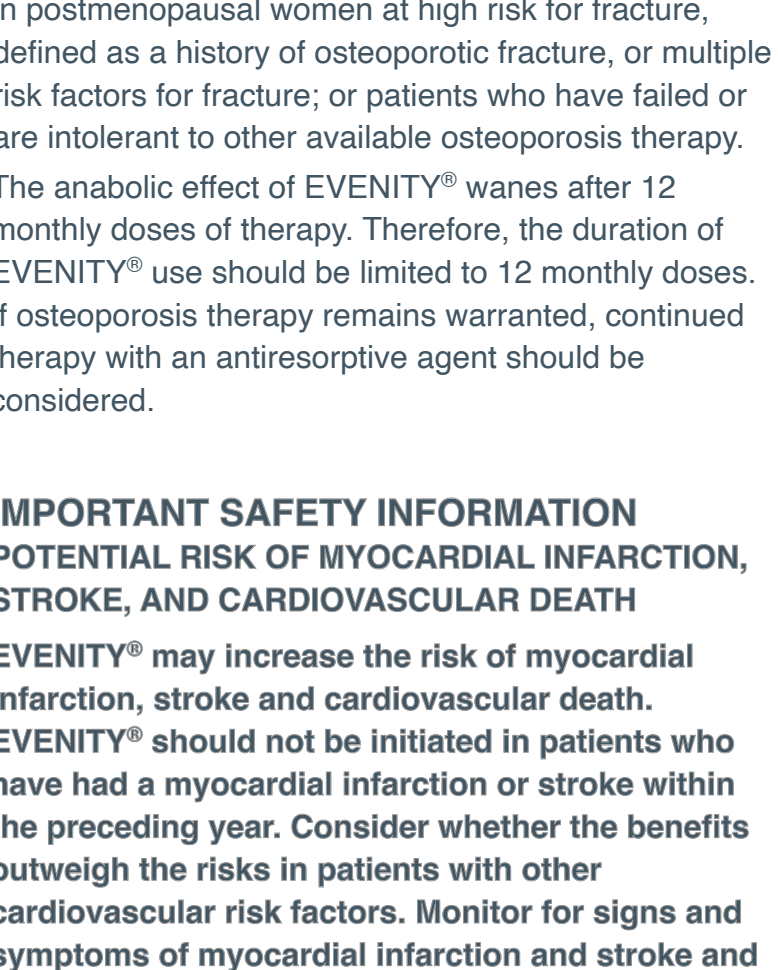
Please scroll below for additional Important Safety Information.

Dear [Insert Customer Name],

The ARCH Study was a Phase 3, head-to-head, randomized, double-blind, alendronate-controlled study comparing EVENITY® followed by alendronate vs alendronate alone in 4,093 postmenopausal women with osteoporosis who have experienced a fracture. Co-primary endpoints were incidence of morphometric vertebral fracture at 24 months and time to first clinical fracture (nonvertebral and symptomatic vertebral fracture) through the primary analysis period.[1,2]

EVENITY® was compared to a commonly prescribed antiresorptive[2]

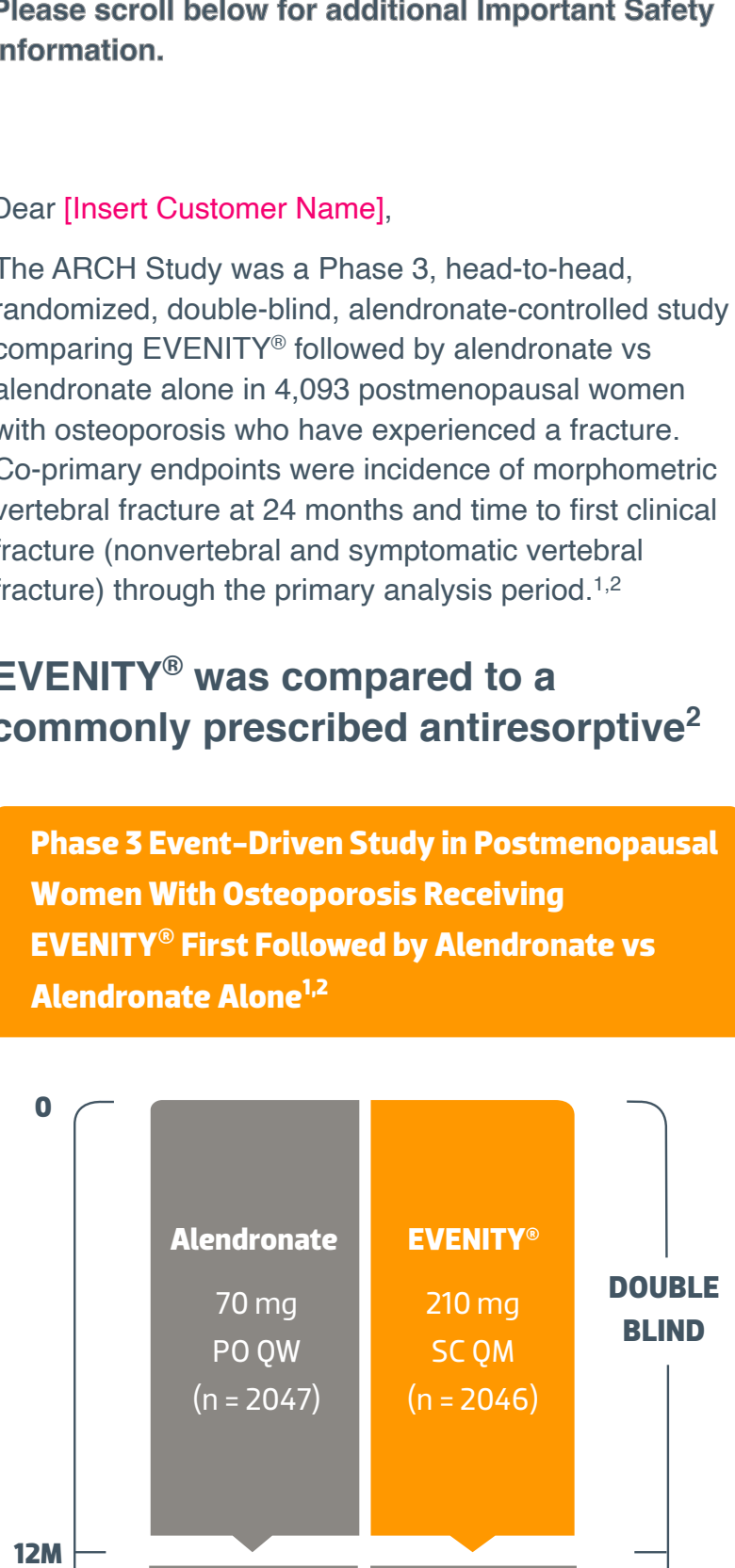
Phase 3 Event-Driven Study in Postmenopausal Women With Osteoporosis Receiving EVENITY® First Followed by Alendronate vs Alendronate Alone[1,2]



The study population consisted of postmenopausal women (55-90 years old). All of the study participants had a bone mineral density (BMD) T-score ≤ -2.5 at the total hip or femoral neck and either one moderate or severe vertebral fracture or two mild vertebral fractures, or BMD T-score ≤ -2.0 at the total hip or femoral neck and either two moderate or severe vertebral fractures or a history of proximal femur fracture. All women were supplemented with daily calcium and vitamin D.[1]

PO=orally; QM=monthly; QW=weekly; SC=subcutaneous.

First Followed by Alendronate vs Alendronate Alone[1,2]



EVENITY® for 12 months followed by alendronate reduced the incidence of clinical fracture (nonvertebral and symptomatic vertebral fracture) at primary analysis (median 33 months) ($P < 0.001$).[1]

This was an event-driven trial and the duration of follow-up varied across subjects. The median duration of subject follow-up for the primary analysis period was 33 months.

*Absolute and relative risk reductions are based on the Mantel-Haenszel method adjusting for age strata, baseline total hip BMD T-score (≤ -2.5, > -2.5), and presence of severe vertebral fracture at baseline.

†*P* value based on logistic regression model (new vertebral fracture) or Cox proportional hazards model (other fracture types) adjusting for age strata, baseline total hip BMD T-score, and presence of severe vertebral fracture at baseline.

‡Nonvertebral fractures excluded fractures of the skull, facial bones, metacarpals, fingers, and toes. Pathologic or high trauma fractures were also excluded.

ARR=absolute risk reduction.

EVENITY® followed by alendronate reduced nonvertebral fracture risk[1,2]

Cumulative Incidence of Nonvertebral and Hip Fractures Through Primary Analysis Period With Median Follow-up of 33 Months
EVENITY® First Followed by Alendronate vs Alendronate Alone[1,2]

This was an event-driven trial and the duration of follow-up varied across subjects. The median duration of subject follow-up for the primary analysis period was 33 months.

§Secondary endpoint.

**Hazard ratio/relative risk reduction and *P* value are based on Cox proportional hazards model adjusting for age strata, baseline total hip BMD T-score, and presence of severe vertebral fracture at baseline.

ARR=absolute risk reduction; BMD=bone mineral density; RRR=relative risk ratio.

Adverse Reactions Occurring in ≥ 2% of EVENITY®-Treated Women in Double-blind Portion of the ARCH Trial[1,††]

Preferred Term	Alendronate (N=2014) n (%)	EVENITY® (N=2040) n (%)
Arthralgia	194 (9.6)	166 (8.1)
Headache	110 (5.5)	106 (5.2)
Muscle spasms	81 (4.0)	70 (3.4)
Edema peripheral	38 (1.9)	34. (1.7)
Asthenia	53 (2.6)	50 (2.5)
Neck pain	42 (2.1)	34(1.7)
Insomnia	36 (1.8)	34(1.7)
Parathesia	34 (1.7)	29 (1.4)

††Adverse reactions based on occurrence in ≥ 2% of EVENITY®-treated patients in either FRAME or ARCH and a plausible relationship to EVENITY®.

Major Adverse Cardiac Events (MACE)[1,‡‡]

During the 12-month double-blind treatment period of the active-controlled trial (ARCH):

- Myocardial infarction[§§] occurred in 16 women (0.8%) in the EVENITY® group and 5 women (0.2%) in the alendronate group
- Stroke[†] occurred in 13 women (0.6%) in the EVENITY® group and 7 women (0.3%) in the alendronate group
- Cardiovascular death*** occurred in 17 women (0.8%) in the EVENITY® group and 12 women (0.6%) in the alendronate group
- MACE resulted in incidences of 41 (2.0%) in the EVENITY® group and 22 (1.1%) in the alendronate group
- ARCH MACE Hazard Ratio: 1.87 (1.11, 3.14) for EVENITY® compared to alendronate

‡‡MACE is a composite endpoint of positively adjudicated myocardial infarction, stroke, and cardiovascular death.

§§These events occurred in patients with and without a history of myocardial infarction or stroke.

***Includes fatal events adjudicated as CV-related or undetermined.

CV=cardiovascular; MI=myocardial infarction.

Consider EVENITY® first after fracture when your members' risk of another is at its highest.[1,3]

Please visit EVENITYHCP.com for more information.

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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 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 (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 Medication Guide.

References:

1. EVENITY® (romosozumab-aqqg) prescribing information, Amgen. **2.** Saag KG, Petersen J, Brandi ML, Karaplis AC, Lorentzon M, Thomas T, et al. Romosozumab or alendronate for fracture prevention in women with osteoporosis. *N Engl J Med.* 2017;377:1417-1427. **3.** van Geel TACM, van Helden S, Geusens PP, Winkens B, Dinant G-J. Clinical subsequent fractures cluster in time after first fractures. *Ann Rheum Dis.* 2009;68:99-102.

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