Managed Healthcare[®]

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 alone¹

continued therapy with an antiresorptive agent should be considered.

injection 105 mg/1,17 mL

(romosozumab-aggg)

fracture) through the primary analysis period.^{1,2}

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osteoporosis therapy.

INDICATION

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, IMPORTANT SAFETY INFORMATION

postmenopausal women at high risk for fracture, defined as a history

EVENITY® is indicated for the treatment of osteoporosis in

of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available

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

seek prompt medical attention if symptoms occur. If a patient experiences a myocardial infarction or stroke during therapy, EVENITY® should be discontinued.

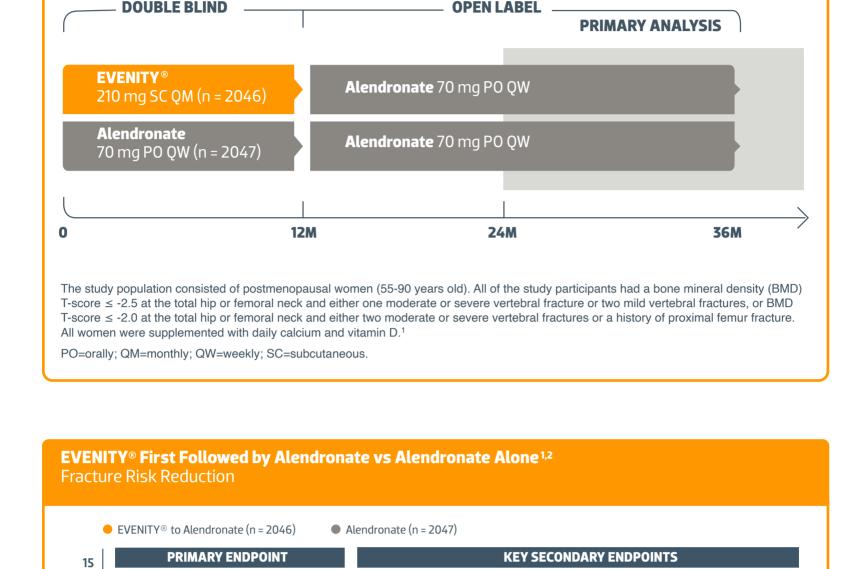
Please scroll below for additional Important Safety Information. Dear [Insert Customer Name], The ARCH Study was a Phase 3, head-to-head, randomized, double-blind, alendronate-controlled study comparing EVENITY® followed by alendronate vs alendronate alone in 4,093 postmenopausal women with osteoporosis who have experienced a fracture. Co-primary endpoints were incidence of morphometric

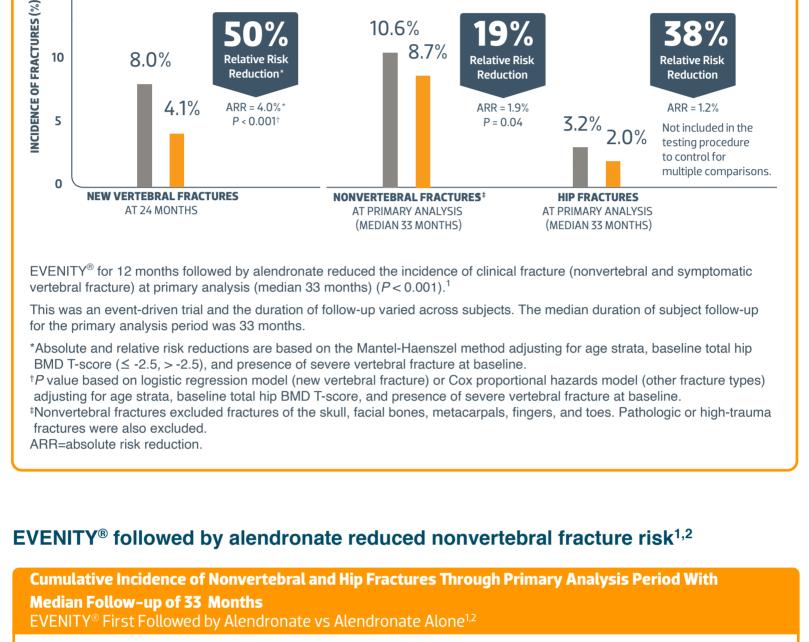
vertebral fracture at 24 months and time to first clinical fracture (nonvertebral and symptomatic vertebral

factors. Monitor for signs and symptoms of myocardial infarction and stroke and instruct patients to

Phase 3 Event-Driven Study in Postmenopausal Women With Osteoporosis Receiving **EVENITY®** First Followed by Alendronate vs Alendronate Alone^{1,2}

EVENITY® was compared to a commonly prescribed antiresorptive²

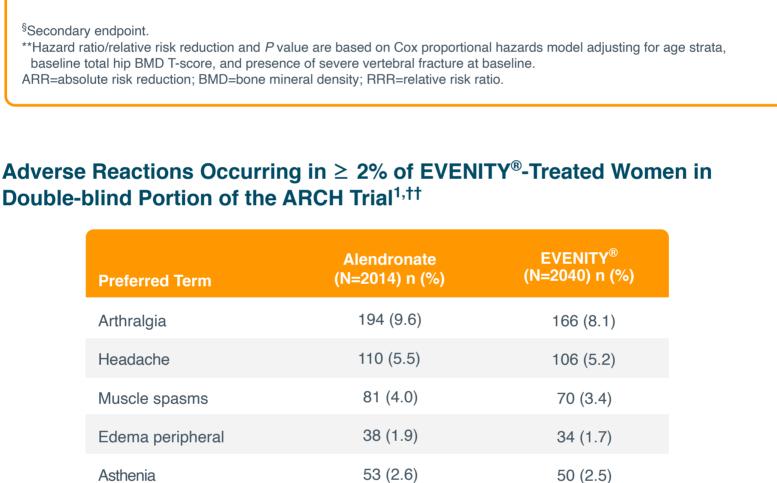




12M 18M 30M 42M 48M **6M** 12M 18M 24M 30M 36M 24M 36M

42M

48M



42 (2.1)

36 (1.8)

34 (1.7)

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

^{††}Adverse reactions based on occurrence in ≥ 2% of EVENITY®-treated patients in either FRAME

34 (1.7)

34 (1.7)

29 (1.4)

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

• ARCH MACE Hazard Ratio: 1.87 (1.11, 3.14) for EVENITY® compared to

#MACE is a composite endpoint of positively adjudicated myocardial infarction, stroke, and

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

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

IMPORTANT SAFETY INFORMATION

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.

have included angioedema, erythema multiforme, and urticaria.

CV=cardiovascular; MI=myocardial infarction.

Neck pain

Parathesia

or ARCH and a plausible relationship to EVENITY®.

Major Adverse Cardiac Events (MACE)^{1,‡‡}

5 women (0.2%) in the alendronate group

in the alendronate group

alendronate

cardiovascular death.

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®.

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.

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

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

Please see EVENITY® full <u>Prescribing Information</u>, including <u>Medication Guide</u>.

time after first fractures. Ann Rheum Dis. 2009;68:99-102.

Amgen Inc.

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

References: 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

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••• EVENITY® to Alendronate Alendronate to Alendronate FIRST HIP FRACTURES FIRST NONVERTEBRAL FRACTURES PATIENT EXPERIENCING EVENT (%) PATIENT EXPERIENCING EVENT (%)RRR = 19%* RRR = 38%* ARR = 1.9% ARR = 1.2% Does not meet 10 multiplicity-adjusted statistical significance 5 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.

• Stroke[†] occurred in 13 women (0.6%) in the EVENITY[®] group and 7 women (0.3%) • MACE resulted in incidences of 41 (2.0%) in the EVENITY® group and 22 (1.1%)

POTENTIAL RISK OF MYOCARDIAL INFARCTION, STROKE, AND CARDIOVASCULAR DEATH EVENITY® may increase the risk of myocardial infarction, stroke and cardiovascular death. EVENITY®

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

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

Hypersensitivity: Hypersensitivity reactions, including angioedema, erythema multiforme, dermatitis, rash, and urticaria have occurred in EVENITY®-treated patients. If an anaphylactic or other clinically significant

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.

stroke, in patients treated with EVENITY® compared to those treated with alendronate.

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

Please visit <u>EVENITYHCP.com</u> for more information.

surgeon. In these patients, dental surgery to treat ONJ may exacerbate the condition. Discontinuation of EVENITY® should be considered based on benefit-risk assessment.

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

1. EVENITY® (romosozumab-aqqg) prescribing information, Amgen. 2. Saag KG, Petersen J, Brandi ML, Karaplis AC, Lorentzon M,

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and headache.

immunogenicity.