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

AMGEN Assist®
Telephone: 1-877-776-5421
Fax: 1-877-877-6542

Claims Tracking Support Request Form

For claims tracking assistance, please complete this form and return via fax to Amgen Assist® at **1-877-877-6542**. Upon Receipt, an Amgen Assist® coordinator will follow up with the payor(s) to obtain the status of the claim.

New and Existing Patients

Patient Name: Patient Date of Birth:

Patient Record ID: PP_____
If available, Patient Record ID can be found on the upper right-hand corner of the Summary of Benefits

Copy of Claim Attached (check one): ☐ Yes ☐ No

Attach Copy of Insurance Card (primary and secondary, if applicable)

Provider Demographics (not required if patient is on file at Amgen Assist®)

Physician Name:

Site Name:

Site Street Address:

City, State and ZIP:

Site Phone Number: Site Fax:

Site Contact for Claims Follow-up:

Contact Phone Number (if different than above):

Physician or Group NPI:

Tax ID:

Medicare PTAN Number (Medicare claims only):

Claim Information (Complete below OR fax copy of claim)

EVENITY™ HCPCS (J- Code) Code: EVENITY™ Billed Amount:

Administration Code: Administration Billed Amount:

Date of Service: Date Claim Submitted to Payor:

Tracking Requested for (check one): Primary Insurance ☐ Secondary Insurance ☐ All ☐

Please see accompanying Brief Summary including Boxed Warning.

Return via fax to **Amgen Assist® at 1-877-877-6542**

USA-785-80250

EVENITY™ (romosozumab-aqqg) injection, for subcutaneous use

BRIEF SUMMARY OF PRESCRIBING INFORMATION
Please see package insert for full Prescribing Information

WARNING: 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. If a patient experiences a myocardial infarction or stroke during therapy, EVENITY should be discontinued.**

1. INDICATIONS AND USAGE

1.1 Treatment of Postmenopausal Women with Osteoporosis at High Risk for Fracture

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.

1.2 Limitations 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 anti-resorptive agent should be considered.

4. CONTRAINDICATIONS

EVENITY is contraindicated in patients with:

- Hypocalcemia. Pre-existing hypocalcemia must be corrected prior to initiating therapy with EVENITY.
- A history of systemic hypersensitivity to romosozumab or to any component of the product formulation. Reactions have included angioedema, erythema multiforme, and urticaria.

5. WARNINGS AND PRECAUTIONS

5.1 Major Adverse Cardiac Events (MACE)

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.

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.

5.2 Hypersensitivity Reactions

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.

5.3 Hypocalcemia

Hypocalcemia has occurred in patients receiving EVENITY. Correct hypocalcemia prior to initiating EVENITY. Monitor patients for signs and symptoms of hypocalcemia. Patients should be adequately supplemented with calcium and vitamin D while on EVENITY.

Patients with severe renal impairment (estimated glomerular filtration rate [eGFR] 15 to 29 mL/min/1.73 m^2) or receiving dialysis are at greater risk of developing hypocalcemia. Monitor serum calcium and adequately supplement patients who have severe renal impairment or are receiving dialysis with calcium and vitamin D. Instruct patients with severe renal impairment, including those receiving dialysis, about the symptoms of hypocalcemia and the importance of maintaining calcium levels with adequate calcium and vitamin D supplementation.

5.4 Osteonecrosis of the Jaw

Osteonecrosis of the jaw (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 examination should be performed by the prescriber prior to initiation of EVENITY treatment. 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 of the treating physician and/or oral surgeon should guide the management plan of each patient based on benefit-risk assessment. Patients who are suspected of having or who develop ONJ while on EVENITY 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.

5.5 Atypical Subtrochanteric and Diaphyseal Femoral Fractures

Atypical low-energy or low trauma fractures of the femoral shaft have been reported in patients receiving EVENITY. These fractures can occur anywhere in the femoral shaft from just below the lesser trochanter to above the supracondylar flare and are transverse or short oblique in orientation without evidence of comminution. Causality has not been established as these fractures also occur in osteoporotic patients who have not been treated.

Atypical femoral fractures most commonly occur with minimal or no trauma to the affected area. They may be bilateral and many patients report prodromal pain in the affected area, usually presenting as dull, aching thigh pain, weeks to months before a complete fracture occurs.

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 suspected of having an atypical fracture and should be evaluated to rule out an incomplete femur fracture. Patient presenting with an atypical femur fracture should also be assessed for symptoms and signs of fracture in the contralateral limb. Interruption of EVENITY therapy should be considered based on benefit-risk assessment.

6. ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the label:

- Major adverse cardiac events
- Hypersensitivity
- Hypocalcemia
- Osteonecrosis of the Jaw
- Atypical Subtrochanteric and Diaphyseal Femoral Fractures

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of EVENITY for the treatment of postmenopausal osteoporosis was evaluated in a multicenter, randomized, double-blind, placebo-controlled study (Study 1, NCT01575834) of 7180 postmenopausal women aged 55 to 90 years (mean age of 71 years). A total of 3581 and 3576 women received at least one dose of EVENITY and placebo, respectively, administered once every month during the 12-month double-blind study period. Women received at least 500 mg calcium and 600 international units of vitamin D supplementation daily and 77% received a loading dose of 50,000 to 60,000 international units of vitamin D within one week of randomization (if serum 25-hydroxyvitamin D concentrations were 40 ng/mL or less).

The safety of EVENITY for the treatment of postmenopausal osteoporosis in patients at high risk of fracture was evaluated in a multicenter, randomized, double-blind, alendronate-controlled study (Study 2, NCT01631214) of 4093 postmenopausal women aged 55 to 90 years (mean age of 74 years). A total of 2040 and 2014 women received at least one dose of EVENITY and alendronate, respectively, during the 12-month double-blind study period. Women received at least 500 mg calcium and 600 international units vitamin D supplementation daily and 74% received a loading dose of 50,000 to 60,000 international units of vitamin D within one week of randomization (if serum 25-hydroxyvitamin D concentrations were 40 ng/mL or less).

In Study 1, during the 12-month double-blind treatment period, the incidence of all-cause mortality was 0.7% (24/3576) in the placebo group and 0.8% (29/3581) in the EVENITY group. The incidence of nonfatal serious adverse events was 8.3% in the placebo group and 9.1% in the EVENITY group. The percentage of patients who withdrew from the study due to adverse events was 1.1% in the placebo group and 1.1% in the EVENITY group. The most common adverse reactions reported with EVENITY (greater than or equal to 5% and at a higher incidence than placebo) were arthralgia and headache. The most common adverse reaction leading to discontinuation of EVENITY was arthralgia (6 subjects [0.2%] in the placebo group and 5 subjects [0.1%] in the EVENITY group).

In Study 2, during the 12-month double-blind treatment period, the incidence of all-cause mortality was 1.1% (22/2014) in the alendronate group and 1.5% (30/2040) in the EVENITY group. The incidence of nonfatal serious adverse events was 13.3% in the alendronate group and 11.9% in the EVENITY group. The percentage of patients who withdrew from the study due to adverse events was 1.2% in the alendronate group and 1.2% in the EVENITY group. The most common adverse reactions reported with EVENITY (greater than or equal to 5%) were arthralgia and headache.

Table 1 outlines the most common adverse reactions occurring in greater than or equal to 2% of EVENITY treated women in at least one study.

Table 1 Adverse Reactions Occurring in ≥ 2% of EVENITY-Treated Women in at Least One Study (Studies 1 and 2)

	Study 1		Study 2	
Preferred Term	Placebo (N = 3576) n (%)	EVENITY (N = 3581) n (%)	Alendronate (N = 2014) n (%)	EVENITY (N = 2040) n (%)
Arthralgia	434 (12.1)	468 (13.1)	194 (9.6)	166 (8.1)
Headache	208 (5.8)	235 (6.6)	110 (5.5)	106 (5.2)
Muscle spasms	140 (3.9)	163 (4.6)	81 (4.0)	70 (3.4)
Edema peripheral	67 (1.9)	86 (2.4)	38 (1.9)	34 (1.7)
Asthenia	79 (2.2)	84 (2.3)	53 (2.6)	50 (2.5)
Neck pain	54 (1.5)	80 (2.2)	42 (2.1)	34 (1.7)
Insomnia	68 (1.9)	72 (2.0)	36 (1.8)	34 (1.7)
Paresthesia	62 (1.7)	72 (2.0)	34 (1.7)	29 (1.4)

The adverse reactions described below are from the 12-month treatment periods of Study 1 (placebo-controlled) and Study 2 (alendronate-controlled).

Major Adverse Cardiac Events (MACE)

During the 12-month double-blind treatment period of the placebo-controlled trial (Study 1), myocardial infarction occurred in 9 women (0.3%) in the EVENITY group and 8 (0.2%) women in the placebo group; stroke occurred in 8 women (0.2%) in the EVENITY group and 10 (0.3%) women in the placebo group. These events occurred in patients with and without a history of myocardial infarction or stroke. Cardiovascular death occurred in 17 women (0.5%) in the EVENITY group and 15 (0.4%) women in the placebo group. The number of women with positively adjudicated MACE was 30 (0.8%) in the EVENITY group and 29 (0.8%) in the placebo group, yielding a hazard ratio of 1.03 (95% confidence interval [0.62, 1.72]) for EVENITY compared to placebo.

During the 12-month double-blind treatment period of the active-controlled trial (Study 2), myocardial infarction occurred in 16 women (0.8%) in the EVENITY group and 5 (0.2%) women in the alendronate group; stroke occurred in 13 women (0.6%) in the EVENITY group and 7 (0.3%) women in the alendronate group. These events occurred in patients with and without a history of myocardial infarction or stroke. Cardiovascular death occurred in 17 women (0.8%) in the EVENITY group and 12 (0.6%) women in the alendronate group. The number of women with positively adjudicated MACE was 41 (2.0%) in the EVENITY group and 22 (1.1%) in the alendronate group, yielding a hazard ratio of 1.87 (95% confidence interval [1.11, 3.14]) for EVENITY compared to alendronate.

Hypersensitivity Reactions

Across both trials, hypersensitivity reactions were reported in 364 (6.5%) women in the EVENITY group and 365 (6.5%) women in the control group. Reported reactions included angioedema (3 women [< 0.1%] in the EVENITY group vs. 3 [< 0.1%] women in the control group), erythema multiforme (1 woman [< 0.1%] in the EVENITY group vs. no woman in the control group), dermatitis (32 women [0.6%] in the EVENITY group vs. 42 women [0.8%] in the control group), rash (60 women [1.1%] in the EVENITY group vs. 53 women [0.9%] in the control group), and urticaria (23 women [0.4%] in the EVENITY group vs. 27 women [0.5%] in the control group). Although angioedema, dermatitis and urticaria were not reported at a higher incidence with EVENITY than control, there were cases of angioedema, dermatitis and urticaria that were determined to be related to EVENITY use.

Hypocalcemia

Across both trials, adverse events of hypocalcemia occurred in 2 EVENITY-treated women and in 1 woman in the control group. Decreases in albumin-adjusted serum calcium to below the lower limit of the reference range (8.3 mg/dL) were reported in 14 (0.2%) women in the EVENITY group and 10 (0.2%) women in the control group. No patient receiving EVENITY developed serum calcium less than 7.5 mg/dL. The nadir in albumin-adjusted serum calcium occurred by month 1 after EVENITY dosing in patients with normal renal function.

Injection Site Reactions

Across both trials, injection site reactions occurred in 278 (4.9%) women in the EVENITY group and 157 (2.8%) women in the control group. The most common injection site reactions were pain (94 [1.7%] women in the EVENITY group; 70 [1.3%] in the control group) and erythema (80 [1.4%] women in the EVENITY group and 14 [0.3%] women in the control group). Injection site reactions resulted in discontinuation of treatment in 7 (0.1%) EVENITY-treated patients and 3 (< 0.1%) patients in the control group.

Osteonecrosis of the Jaw

Across both trials, osteonecrosis of the jaw occurred in one patient during treatment with EVENITY.

Atypical Subtrochanteric and Diaphyseal Fractures

Across both trials, atypical femoral fracture occurred in one patient during treatment with EVENITY.

6.2 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies in the studies described below with the incidence of antibodies in other studies or to other romosozumab products may be misleading.

The immunogenicity of EVENITY was evaluated using an immunoassay for the detection of anti-romosozumab-aqqg antibodies. An *in vitro* biological assay was performed to detect neutralizing antibodies for those subjects whose sera tested positive for anti-romosozumab-aqqg antibodies.

Among 5914 postmenopausal women treated with EVENITY 210 mg monthly, 18.1% of subjects developed antibodies to romosozumab-aqqg. Of the subjects who developed antibodies to romosozumab-aqqg, 4.7% had antibodies that were classified as neutralizing. Development of antibodies to romosozumab-aqqg was associated with lower serum romosozumab-aqqg concentrations. Antibodies to romosozumab-aqqg were generally not associated with changes in the efficacy or safety of EVENITY.

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

EVENITY is not indicated for use in women of reproductive potential. In animal reproduction studies, weekly administration of romosozumab-aqqg to pregnant rats during the period of organogenesis at exposures greater than 32 times the clinical exposure produced skeletal abnormalities in the offspring. Administration of romosozumab-aqqg to rats prior to mating and through to the end of lactation produced minimal to slight decreases in femoral bone mineral density and/or cortical circumferences in the offspring at 1.5 to 56 times the expected exposure in humans.

Data

Animal Data

Reproductive and developmental effects of romosozumab-aqqg were assessed in the rat in a preliminary and definitive embryo-fetal development study, a combined fertility and embryo-development study, and a pre- and postnatal development study.

Skeletal malformations including syndactyly and polydactyly occurred in 1 out of 75 litters across all rat reproductive toxicity studies, in the litter of a dam given weekly subcutaneous romosozumab-aqqg doses of 300 mg/kg (equivalent to at least 32 times the clinical exposure observed in humans following a monthly subcutaneous dose of 210 mg, based on area under the concentration-time curve [AUC] comparison).

In the offspring of female rats given weekly romosozumab-aqqg doses from 6 weeks before cohabitation through mating and lactation, femoral periosteal and endocortical circumferences were slightly decreased at 10, 60, and 300 mg/kg (equivalent to 1.5, 19, and 56 times the clinical exposure following a monthly subcutaneous dose of 210 mg, based on AUC comparison). Cortical thickness was increased at 300 mg/kg (equivalent to 56 times expected clinical exposure). Femoral metaphyseal bone mineral density was slightly decreased at 60 and 300 mg/kg (equivalent to 19 and 56 times expected clinical exposure).

8.2 Lactation

Risk Summary

EVENITY is not indicated for use in women of reproductive potential. In animal studies where pregnant rats were given weekly doses of romosozumab-aqqg from 6 weeks before cohabitation through mating and lactation at 10, 60, or 300 mg/kg (equivalent to 1.5, 19 or 56 times the clinical exposure following a monthly subcutaneous dose of 210 mg, based on AUC comparison), romosozumab-aqqg was dose-dependently present in the serum of offspring on postnatal day 21 at 0.01 to 2.4 times maternal exposure due to gestational and/or lactational exposure.

8.4 Pediatric Use

Safety and effectiveness of EVENITY have not been established in pediatric patients.

8.5 Geriatric Use

Of the 6544 postmenopausal women with osteoporosis in the clinical studies of EVENITY, 5234 (80%) were age 65 years and over and 2390 (37%) were age 75 years and over. No overall differences in safety or efficacy were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in response between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

8.7 Renal Impairment

No dose adjustment is needed in patients with renal impairment.

Patients with severe renal impairment (estimated glomerular filtration rate [eGFR] 15 to 29 mL/min/1.73 m^2 by MDRD equation) or receiving dialysis are at greater risk of developing hypocalcemia. Monitor calcium concentrations and adequately supplement calcium and vitamin D in patients who have severe renal impairment or are receiving dialysis.

13. NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity

In a rat carcinogenicity study, once-weekly romosozumab-aqqg doses of 3, 10 or 50 mg/kg were administered by subcutaneous injection to Sprague-Dawley rats from 8 weeks up to 98 weeks of age, resulting in systemic exposures that were up to 19 times the systemic exposure observed in humans following a monthly subcutaneous dose of 210 mg EVENITY (based on AUC comparison). Romosozumab-aqqg caused a dose-dependent increase in bone mass with trabecular and cortical bone thickening at all doses. There were no effects of romosozumab-aqqg on mortality and romosozumab-aqqg did not cause significant increases in tumor incidence in male or female rats.

Mutagenicity

Mutagenesis has not been evaluated, as monoclonal antibodies are not expected to alter DNA or chromosomes.

Impairment of Fertility

No effects on fertility were observed in male and female rats given subcutaneous romosozumab-aqqg doses up to 300 mg/kg (up to 56 times the systemic exposure observed in humans following a monthly subcutaneous dose of 210 mg EVENITY, based on AUC comparison). No effects were noted in reproductive organs in rats and cynomolgus monkeys dosed subcutaneously for 6 months with weekly doses up to 100 mg/kg (exposures up to 38 and 93 times, respectively, the systemic exposure observed in humans administered monthly subcutaneous doses of 210 mg based on AUC comparison).

13.2 Animal Toxicology and Pharmacology

No adverse effects were noted in rats and monkeys after 26 once-weekly subcutaneous romosozumab-aqqg doses up to 100 mg/kg, equivalent to systemic exposures of 38 and 93 times, respectively, the systemic exposure observed in humans following a monthly subcutaneous dose of 210 mg EVENITY (based on AUC comparison).

Bone safety studies of up to 12-month duration were conducted in ovariectomized rats and monkeys with once-weekly romosozumab-aqqg doses yielding exposures ranging from 1 to 22 times the systemic exposure in humans given monthly doses of 210 mg, based on AUC comparison. Romosozumab-aqqg increased bone mass and improved cancellous bone microarchitecture and cortical bone geometry by increasing bone formation on periosteal, endocortical, and trabecular surfaces, and decreasing bone resorption on trabecular and endocortical surfaces. The increases in bone mass were significantly correlated with increases in bone strength. In rats and monkeys, bone quality was maintained at all skeletal sites at doses ranging from 1 to 22 times human exposure, and slightly improved in vertebrae at 19 to 22 times human exposure. There was no evidence of mineralization defects, osteoid accumulation, or woven bone formation.

The risk information provided here is not comprehensive. The FDA-approved product labeling can be found at www.evenityhcp.com or contact Amgen Medical Information at 1-800-772-6436.

EVENITY™ (romosozumab-aqqg)
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v1