EVENITY® (romosozumab) Brief Prescribing information Please refer to the Summary of Product Characteristics before prescribing Evenity. **PHARMACEUTICAL FORM** EVENITY (romosozumab) injection is supplied as a sterile, preservative free, clear to opalescent, colorless to light yellow solution for subcutaneous injection in a single use prefilled syringe. **CLINICAL PARTICULARS Therapeutic indications** Treatment of Postmenopausal Women with Osteoporosis at High Risk for Fractur. 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. **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. **Posology and method of administration Important Dosage and Administration Instructions** Two separate syringes (and two separate subcutaneous injections) are needed to administer the total dose of 210 mg of EVENITY. Inject two 105 mg/1.17 mL prefilled syringes, one after the other. EVENITY should be administered by a healthcare provider. **Recommended Dosage** The recommended dose of EVENITY is 210 mg administered subcutaneously in the abdomen, thigh or upper arm. Administer EVENITY once every month. The treatment duration for EVENITY is 12 monthly doses. Patients should be adequately supplemented with calcium and vitamin D during treatment with EVENITY. if the EVENITY dose is missed, administer as soon as it can be rescheduled. Thereafter, EVENITY can be scheduled every month from the date of the last dose. **Preparation and Administration Instructions Step 1: Prior to Administration:** Remove two syringes from the carton. Visually inspect EVENITY for particles and discoloration prior to administration. EVENITY is a clear to opalescent, colorless to light yellow solution. Do not use if the solution is cloudy or discolored or contains particles. Do not use the syringe if any part appears cracked or broken. the gray needle cap is missing or not securely attached. the expiration date printed on the label has passed. Always hold the prefilled syringe by the syringe barrel to remove the syringe from the tray. See Figure A. Do not grasp the plunger rod. Do not grasp the gray needle cap. Do not remove the gray needle cap until you are ready to inject. Allow EVENITY to sit at room temperature for at least 30 minutes before injecting. Do not warm in any other way. **Step 2: Select the Injection Site and Prepare the Syringe** Prepare and clean two injection sites, one for each of the two injections. The recommended subcutaneous injection sites include: The thigh. Abdomen, except for a two-inch area right around the navel. Outer area of upper arm. Clean the injection sites with alcohol wipes. Let the skin dry. Choose a different site each time you give an injection. If you want to use the same injection site, make sure it is not the same spot on the injection site you used for a previous injection. Do not inject into areas where the skin is tender, bruised, red, or hard. Avoid injecting into areas with scars or stretch marks. Choose the first syringe. Pull the gray needle cap straight off and away from your body when you are ready to inject. Do not put the gray needle cap back onto the syringe. **Step 3: Inject EVENIT** Insert needle and inject all the liquid subcutaneously. Do not administer into muscle or blood vessel. See Figure D. When done, gently lift the syringe off of the skin. **Step 4: Syringe and Needle Cap Disposal** Immediately dispose of the syringe and needle cap in the nearest sharps container **Important: Repeat all steps with the second syringe to inject the full dose. 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 **Special warnings and precautions for us** 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 **Hypersensitivity Reaction** 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 **Hypocalcemi** 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 m2) 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. **Osteonecrosis of the Ja** 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. **Atypical Subtrochanteric and Diaphyseal Femoral Fracture** 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 **Sodium content** This medicinal product contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially sodium-free. **Special populations. Pediatric Us** Safety and effectiveness of EVENITY have not been established in pediatric patients. **Geriatric Us** 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. **Renal Impairment** No dose adjustment is required in patients with renal impairment. Patients with severe renal impairment (estimated glomerular filtration rate [eGFR] 15 to 29 mL/min/1.73 m2 by MDRD equation) or receiving dialysis are at greater risk of developing hypocalcemia [see Contraindications (4), Warnings and Precautions (5.3) and Adverse Reactions (6.1)]. Monitor calcium concentrations and adequately supplement calcium and vitamin D in patients who have severe renal impairment or are receiving dialysis. **Interaction with other medicinal products and other forms of interaction** No drug interaction studies have been performed with romosozumab. No pharmacokinetic drug interactions are expected with romosozumab. **Fertility, pregnancy and lactation Pregnancy** Risk Summary EVENITY is not indicated for use in women of reproductive potential. In animal reproduction studies, weekly administration of romosozumab to pregnant rats during the period of organogenesis at exposures greater than 31 times the clinical exposure produced skeletal abnormalities in the offspring. Administration of romosozumab 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 1.4 to 54 times the expected exposure in humans. Data. Animal Data Reproductive and developmental effects of romosozumab 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 doses of 300 mg/kg (equivalent to at least 31 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 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 1.4, 18, and 54 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 54 times expected clinical exposure). Femoral metaphyseal bone mineral density was slightly decreased at 60 and 300 mg/kg (equivalent to 18 and 54 times expected clinical exposure) **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 from 6 weeks before cohabitation through mating and lactation at 10, 60, or 300 mg/kg (equivalent to 1.4, 18 or 54 times the clinical exposure following a monthly subcutaneous dose of 210 mg, based on AUC comparison), romosozumab 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. **Effects on ability to drive and use machines** Romosozumab has no or negligible influence on the ability to drive and use machines. **Undesirable effects** 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. **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 antibodies. An in vitro biological assay was performed to detect neutralizing antibodies for those subjects whose sera tested positive for anti-romosozumab antibodies.Among 5914 postmenopausal women treated with EVENITY 210 mg monthly, 18.1% of subjects developed antibodies to romosozumab. Of the subjects who developed antibodies to romosozumab, 4.7% had antibodies that were classified as neutralizing. Development of antibodies to romosozumab was associated with lower serum romosozumab concentrations. Antibodies to romosozumab were generally not associated with changes in the efficacy or safety of EVENITY. **Overdose** There is no experience with overdose in clinical trials. There is no known antidote to romosozumab or specific treatment for overdose. In case of overdose, it is recommended that patients are monitored closely and given appropriate treatment. **Special precautions for storage** Refrigerate EVENITY at 2°C to 8°C in the original carton to protect from light. Do not freeze. Do not shake. If removed from the refrigerator, EVENITY can be kept at room temperature up to 25°C in the original carton and must be used within 30 days. If not used within 30 days, discard EVENITY. Do not expose EVENITY to temperatures above 25°C. **Special precautions for disposal and other handling** The solution should be visually inspected for particles and discoloration prior to administration. EVENITY should not be used if the solution is discolored, cloudy, or contains particles. Any unused medicinal product or waste material should be disposed of in accordance with local requirements. **Legal category:** POM **Administrative information: Marketing authorization holder** Amgen Inc. One Amgen Center Drive, Thousand Oaks, California 91320-1799-USA product license Number in Saudi: Evenity 0106210758 date of revision of text: December 2019 Local representative in Saudi Arabia: Salehiya Trading Est. Address: P.O.Box 991, Riyadh 11421, Kingdom of Saudi Arabia. Tel: 00966 1 464 6955 Ext. 127

Any suspected adverse reactions should be reported immediately to Amgen in accordance with local spontaneous reporting requirements. Amgen Fax: +966 11 2799301 or send to mailbox: Safety-MEA@amgen.com and/or National Pharmacovigilance Centre (NPC), Email: npc.drug@sfda.gov.sa , Fax: +966-11-2057662 ,SFDA Call Center 19999, website: http://ade.sfda.gov.sa