EVENITY® (romosozumab)

Prescriber Guide

Important information on minimising risk to ensure safe and effective use

This document has been reviewed and approved by The Saudi Food and Drug Authority (SFDA).

1. ABOUT THIS GUIDE

- 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.
- This guide contains important safety information for healthcare professionals to minimise key risks when prescribing EVENITY.
- The patient or, if appropriate, their caregiver should be educated about treatment risks and provided with a Patient Alert Card.
- Refer to the Summary of Product Characteristics (SmPC) for full prescribing information.

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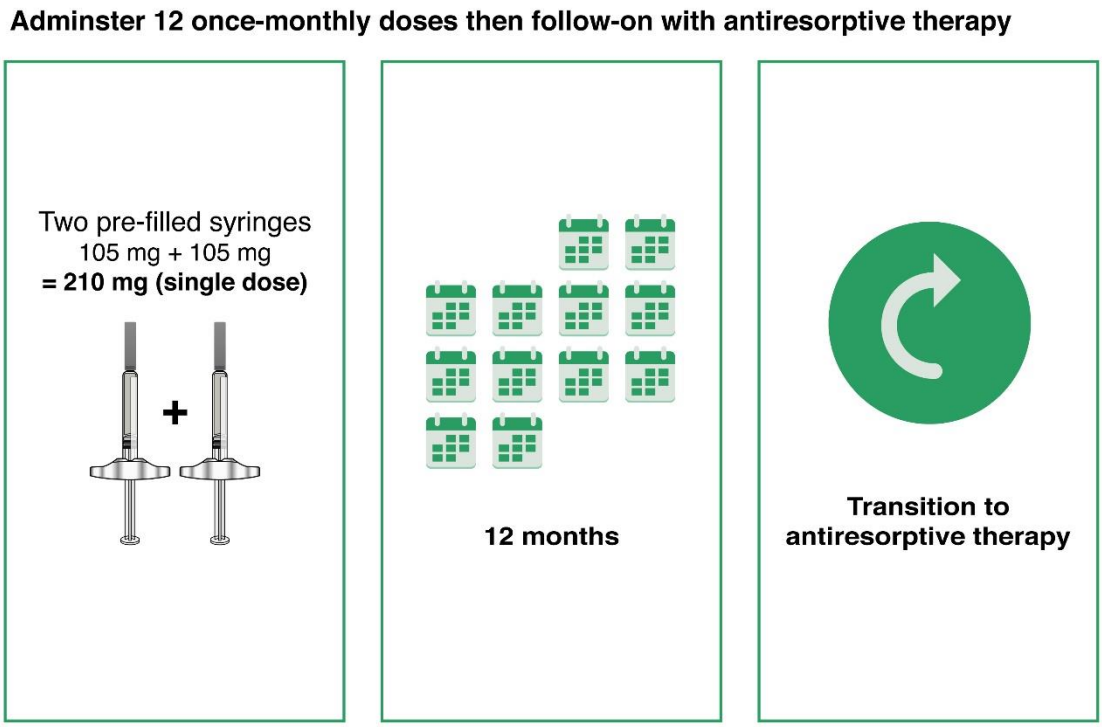
2. ABOUT EVENITY

EVENITY is a bone-building humanized monoclonal antibody that works by inhibiting the action of sclerostin, thereby increasing bone formation and decreasing bone resorption.

A patient should receive the recommended dose of 210 mg (administered as two subcutaneous injections of 105 mg/1.17 ml each) once monthly for 12 months.

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.

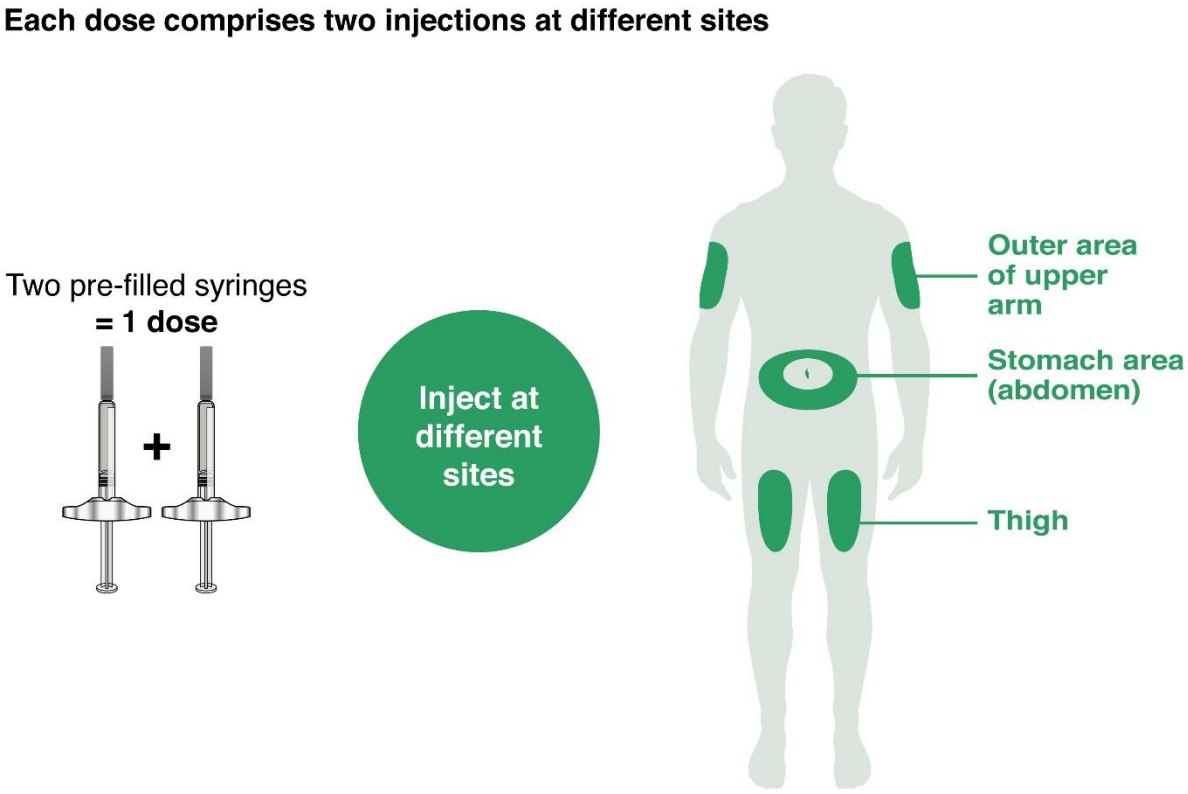


2. ABOUT EVENITY (CONT'D)

EVENITY should be administered by a healthcare provider.

To administer the 210 mg dose, 2 subcutaneous injections of EVENITY should be given into the abdomen, thigh, or outer area of upper arm. The second injection should be given immediately after the first one but at a different injection site.

Further, detailed information on the correct procedure to inject a full dose of EVENITY is provided in the Dosage and Administration section of the SmPC.



3. KEY RISKS

This guide covers the risks of hypocalcaemia and potential risk of myocardial infarction (MI), stroke and cardiovascular death, and the risk of osteonecrosis of the jaw (ONJ), associated with EVENITY use. For detailed information about these and other risks, please refer to the EVENITY SmPC.

- EVENITY is contraindicated in patients with hypocalcaemia. Pre-existing hypocalcemia must be corrected prior to initiating therapy with 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..
- 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
- 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.

Patients should be educated about each of these risks. The next section provides further information.

4. MANAGING KEY RISKS

4.1 HYPOCALCAEMIA

Hypocalcemia has occurred in patients receiving EVENITY.

Management

Hypocalcaemia is a contraindication. Correct hypocalcaemia prior to initiating therapy with EVENITY.

Patients should be adequately supplemented with calcium and vitamin D prior to and during EVENITY treatment.

Monitor patients for signs and symptoms of hypocalcaemia throughout treatment. The predominant features of hypocalcaemia are effects on the nerves and muscles and may include:

- Muscle cramps and/or spasms.
- Paraesthesia of the extremities or periorally.
- Facial twitches.
- Seizures.
- Neuropsychiatric effects, ranging from confusion and disorientation to overt psychosis.

If any patient presents with suspected signs and/or symptoms of hypocalcaemia during treatment, serum calcium levels should be measured.

Patients with severe renal impairment or undergoing dialysis

Patients with severe renal impairment (eGFR 15 to 29 mL/min/1.73 m^2) or receiving dialysis are at greater risk of developing hypocalcaemia and the safety data for these patients is limited. Calcium levels should be monitored in these patients.

4.2 MYOCARDIAL INFARCTION AND STROKE

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.

Background

In two large, controlled fracture trials of romosozumab for the treatment of osteoporosis in postmenopausal women, serious cardiovascular adverse events were prospectively adjudicated.

In an active-controlled trial (n=4054) during the 12-month double-blind treatment phase:

- 16 women (0.8%) had myocardial infarction in the romosozumab arm versus 5 women (0.2%) in the alendronate arm.
- 13 women (0.6%) had stroke in the romosozumab arm versus 7 women (0.3%) in the alendronate arm.

In a placebo-controlled trial (n=7157), no imbalance was observed during the 12-month double-blind treatment phase.

4.3 OSTEONECROSIS OF THE JAW

ONJ is a rare side effect of antiresorptive drugs. It is defined as exposed bone, or bone that can be probed through an intra-oral or extra-oral fistula, in the maxillofacial region, that has persisted for more than eight weeks in patients with a history of treatment with antiresorptive or anti-angiogenic drugs, and where there has been no history of radiation therapy to the jaws or obvious metastatic disease to the jaws.[1]

ONJ has been reported rarely (≥ 1/10,000 to < 1/1,000) in patients receiving EVENITY.

Management

All patients should be encouraged to:

- Immediately report any oral symptoms, such as pain or swelling or non-healing of sores or discharge during treatment with EVENITY.
- Maintain good oral hygiene.
- Receive routine dental check-ups.

If appropriate, consider arranging a dental examination before a patient starts EVENITY treatment.

Patients who are suspected of having or who develop ONJ while on EVENITY should receive care by a dentist or an oral surgeon with expertise in ONJ. Discontinuation of EVENITY therapy should be considered until the condition resolves and contributing risk factors are mitigated where possible. More information on staging and treatment strategies for ONJ are shown in the table.

Risk factors

The following risk factors should be considered when evaluating a patient's risk of developing ONJ:

- Poor oral hygiene, periodontal disease, poorly fitting dentures, history of dental disease, invasive dental procedures, e.g. tooth extractions.
- Potency of the medicinal product that inhibits bone resorption (the risk increases with the antiresorptive potency of the compound), and cumulative dose of bone resorption therapy.
- Cancer, co-morbid conditions (e.g. anaemia, coagulopathies, infection), smoking.
- Concomitant therapies: corticosteroids, chemotherapy, angiogenesis inhibitors, radiotherapy to the head and neck.

5. GENERAL REMINDER LIST

Before prescribing EVENITY, you should ensure:

- ✓ 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.
- ✓ Pre-existing hypocalcemia is corrected prior to initiating therapy with EVENITY.
- ✓ Perform a careful assessment of the cardiovascular risk profile. Consider risk factors such as established cardiovascular disease, hypertension, hyperlipidaemia, diabetes mellitus, smoking, severe renal impairment, and age.
- ✓ Patients are adequately supplemented with calcium and vitamin D before and during treatment, as appropriate.
- ✓ Serum calcium levels are monitored for patients with severe renal impairment or receiving dialysis, who are at increased risk of developing hypocalcaemia.
- ✓ A routine oral examination should be performed by the prescriber prior to initiation of EVENITY treatment.
- ✓ Risk factors for developing osteonecrosis of the jaw are considered, including:
    - Poor oral hygiene, periodontal disease, poorly fitting dentures, history of dental disease, invasive dental procedures, e.g. tooth extractions.
    - Potency of the medicinal product that inhibits bone resorption, and cumulative dose of bone resorption therapy.
    - Cancer, co-morbid conditions (e.g. anaemia, coagulopathies, infection), smoking.
    - Concomitant therapies: corticosteroids, chemotherapy, angiogenesis inhibitors, radiotherapy to the head and neck.
- ✓ The benefit of using EVENITY outweighs the risk.
- ✓ Patients have been provided with the Patient Alert Card and read the Package Leaflet.
- ✓ EVENITY should be administered by a healthcare provider.

6. PATIENT ALERT CARD

Patients or, if appropriate, their caregiver should be educated to reinforce understanding of these risks and the importance of contacting a healthcare professional if they experience suggestive signs and/or symptoms.

A Patient Alert Card should be provided to each patient prescribed EVENITY. This card aids patients in remembering/recognising signs and symptoms of key risks that are associated with EVENITY treatment. It also provides guidance to patients on what they should do should they experience signs and/or symptoms.

Patients should be advised to carry the Patient Alert Card with them at all times and to show it to any healthcare professional who may be treating them.

To obtain additional copies of the Patient Alert Card, please contact Amgen via email to Safety-MEA@amgen.com or call +966 11 2799328.

7. REPORTING ADVERSE REACTIONS

Contact details for adverse event reporting or to request further information. Any suspected adverse reactions should be reported immediately to local Amgen safety contacts or the National Pharmacovigilance and Drug Safety Center.

Amgen Local Safety Contacts
Tel: +966 11 2799328
Email: Safety-MEA@amgen.com

Saudi Food & Drug Authority (SFDA)
The National Pharmacovigilance Center (NPC)
SFDA call center 19999
Toll free phone: 8002490000
Fax: +966 11 2057662
Email: npc.drug@sfda.gov.sa
Online: http://ade.sfda.gov.sa/