EVENITY® (romosozumab) Prescriber Guide

EVENITY®
(romosozumab) injection

Important information on minimising risk to ensure safe and effective use

Approval by HPRA: <October 2024>

Healthcare professionals are asked to report any suspected adverse reactions. These should be reported to HPRA Pharmacovigilance Website: www.hpra.ie Adverse events should also be reported to UCB (Pharma) Ireland Ltd via UCBCares® on 1800 930075 (freephone) or by email UCBCares.IE@ucb.com

1. ABOUT THIS GUIDE

- EVENITY® (romosozumab) is indicated for the treatment of severe osteoporosis in postmenopausal women at high risk of fracture.
- This guide contains important safety information for healthcare professionals to minimise key risks when prescribing romosozumab. The key risks include hypocalcaemia, myocardial infarction (MI) and stroke, and osteonecrosis of the jaw (ONJ).
- 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.
- This educational material is also available at the following website: www.hpra.ie

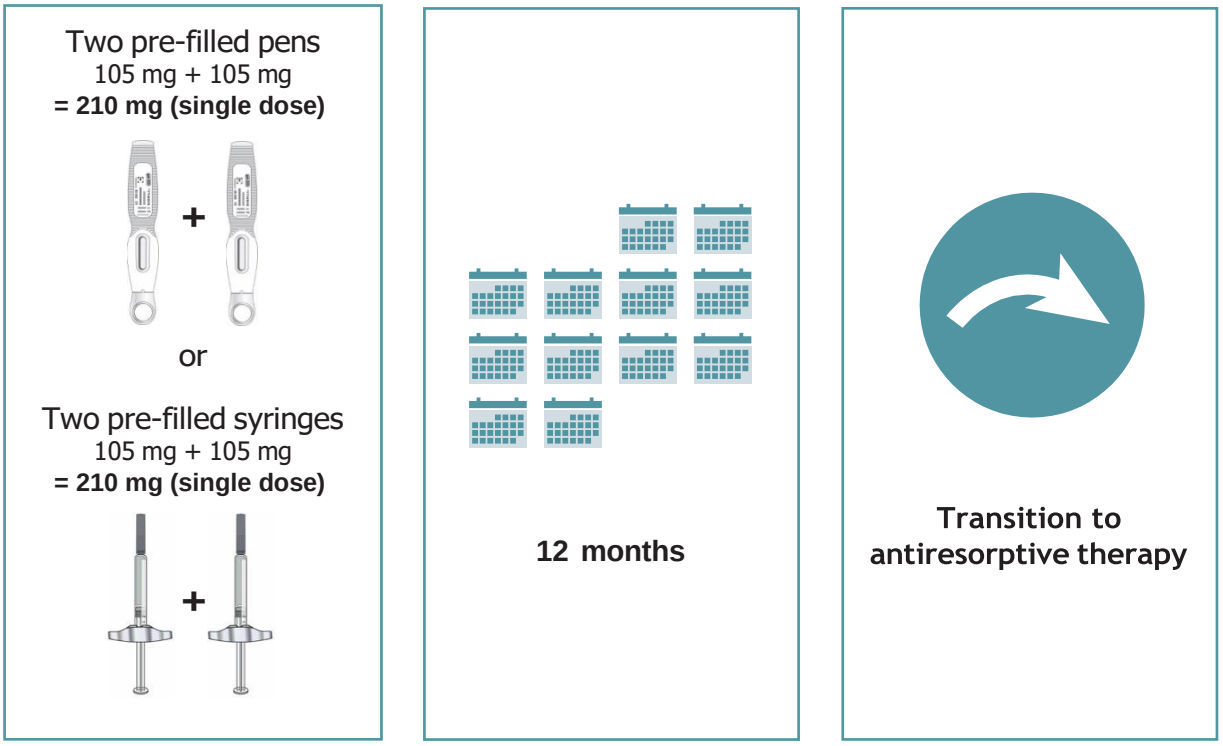
2. ABOUT ROMOSOZUMAB

Romosozumab 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 each) once monthly for 12 months.

Following completion of romosozumab therapy, transition to antiresorptive therapy is recommended in order to extend the benefit achieved with romosozumab beyond 12 months.

Administer 12 once-monthly doses then follow-on with antiresorptive therapy



Romosozumab should only be administered by an individual who has been properly trained in administration of subcutaneous injections.

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

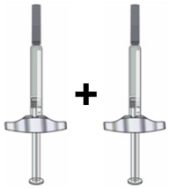
Further, detailed information on the correct procedure to inject a full dose of romosozumab is provided in the Instructions for Use at the back of the package leaflet.

Each dose comprises two injections at different sites

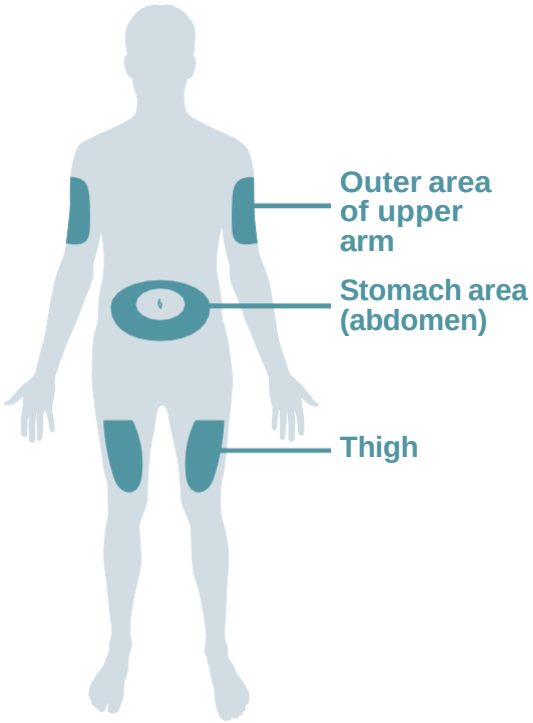
Two pre-filled pens
= 1 dose

or

Two pre-filled syringes
= 1 dose



Inject at different sites



3. KEY RISKS

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

- **Romosozumab is contraindicated in patients with hypocalcaemia. Patients should have their serum calcium levels measured before initiating romosozumab therapy and should be monitored for signs and symptoms of hypocalcaemia throughout treatment.**
- **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.**
- **Romosozumab is contraindicated in patients with history of MI or stroke.**
- **In patients without history of MI or stroke, the individual benefit-risk balance of using romosozumab treatment should be carefully evaluated prior to prescribing.**
- **Risk factors for the development of osteonecrosis of the jaw should be considered and preventative measures encouraged prior to prescribing romosozumab.**

PATIENTS SHOULD BE EDUCATED ABOUT EACH OF THESE RISKS. THE NEXT SECTION PROVIDES FURTHER INFORMATION.

4. MANAGING KEY RISKS

4.1 HYPOCALCAEMIA

Transient hypocalcaemia was observed in patients receiving romosozumab in clinical trials.

Management

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

Patients should be adequately supplemented with calcium and vitamin D prior to and during romosozumab 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 randomised controlled studies, an increase in serious cardiovascular events (myocardial infarction and stroke) has been observed in romosozumab treated patients compared to controls.

Management

Patients with history of MI or stroke: Romosozumab is contraindicated and should not be initiated.

Patients without history of MI or stroke: When determining whether to use romosozumab for an individual patient, consideration should be given to her fracture risk over the next year and her cardiovascular risk based on risk factors (e.g. established cardiovascular disease, hypertension, hyperlipidaemia, diabetes mellitus, smoking, severe renal impairment, age). Romosozumab should only be used if the benefit outweighs the risk.

Patients who develop symptoms suggestive of MI or stroke during romosozumab treatment should undergo a prompt medical evaluation. If a patient experiences a myocardial infarction or stroke during therapy, treatment with romosozumab 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=4093) during the 12-month double-blind treatment phase:

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

In a placebo-controlled trial (n=7180), 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 romosozumab.

Management

All patients should be encouraged to:

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

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

Patients who are suspected of having or who develop ONJ while on romosozumab should receive care by a dentist or an oral surgeon with expertise in ONJ. Discontinuation of romosozumab therapy should be considered until the condition resolves and contributing risk factors are mitigated where possible.

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 anti-resorptive potency of the compound), and cumulative dose of antiresorptive therapy.
- Cancer, co-morbid conditions (e.g. anaemia, coagulopathies, infection), smoking.
- Concomitant therapies: corticosteroids, chemotherapy, angiogenesis inhibitors, radiotherapy to the head and neck.

[1] Ruggiero SL, Dodson TB, Fantasia J, et al. American Association of Oral and Maxillofacial Surgeons position paper on medication-related osteonecrosis of the jaw - 2014 update. Journal of Oral and Maxillofacial Surgery. 2014;72(10):1938-1956.

5. GENERAL REMINDER LIST

Before prescribing romosozumab, you should ensure:

- Serum calcium levels are measured prior to treatment initiation, and hypocalcaemia is corrected before administering romosozumab.
- 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.
- 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 antiresorptive 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 romosozumab outweighs the risk.
- Patients have been provided with the Patient Alert Card and read the package leaflet.
- Patients and/or their caregivers are trained on subcutaneous injection technique if they will administer romosozumab, including the Instructions for Use described in the package leaflet.
- A specific checklist for risk of myocardial infarction and stroke is included in the next section.

6. CHECKLIST FOR RISK OF MYOCARDIAL INFARCTION AND STROKE

Before prescribing romosozumab, you should:

- ☑ Verify that patients do not have a history of myocardial infarction or stroke, which is a contraindication.
- ☑ 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.
- ☑ Ensure that the benefit of using romosozumab outweighs the risk.

7. PATIENT ALERT CARD

Patients or, if appropriate, their caregiver should be educated to reinforce understanding of these risks (i.e. hypocalcemia, MI and stroke, and ONJ) 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 romosozumab. This card aids patients in remembering/recognising signs and symptoms of key risks that are associated with romosozumab 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 UCB (Pharma) Ireland Ltd via UCBCares® on 1800 930075 (freephone) or by email UCBCares.IE@ucb.com

8. REPORTING ADVERSE REACTIONS

Healthcare professionals should report suspected adverse reactions via their national reporting system via the HPRA Pharmacovigilance Website: www.hpra.ie

Please provide as much information as possible when reporting suspected adverse reactions, including comorbidities, past medical history, concomitant medication, and relevant timings and dates.

If you require any further information about the use of romosozumab, please contact UCB (Pharma) Ireland Ltd via UCBCares® on 1800 930075 (freephone) or by email UCBCares.IE@ucb.com