

ANNEX I
SUMMARY OF PRODUCT CHARACTERISTICS

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.

1. NAME OF THE MEDICINAL PRODUCT

EVENTITY 105 mg solution for injection in pre-filled pen
EVENTITY 105 mg solution for injection in pre-filled syringe

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

EVENTITY 105 mg solution for injection in pre-filled pen

Each pre-filled pen contains 105 mg of romosozumab in 1.17 ml of solution (90 mg/ml).

EVENTITY 105 mg solution for injection in pre-filled syringe

Each pre-filled syringe contains 105 mg of romosozumab in 1.17 ml of solution (90 mg/ml).

Romosozumab is a humanized IgG2 monoclonal antibody produced using recombinant DNA technology in Chinese hamster ovary (CHO) cells.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for injection (injection)

Clear to opalescent, colorless to light yellow solution.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

EVENTITY is indicated in treatment of severe osteoporosis in postmenopausal women at high risk of fracture (see section 5.1).

4.2 Posology and method of administration

Treatment should be initiated and supervised by specialist physicians experienced in the management of osteoporosis.

Posology

The recommended dose is 210 mg romosozumab (administered as two subcutaneous injections of 105 mg each) once monthly for 12 months.

Patients should be adequately supplemented with calcium and vitamin D before and during treatment (see sections 4.3 and 4.4).

Patients treated with EVENTITY should be given the package leaflet and the patient alert card.

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

Missed doses

If the romosozumab dose is missed, administer as soon as it can be feasible. Thereafter, the next romosozumab dose should not be given earlier than one month after the last dose.

Special populations

Elderly

No dose adjustment is necessary in elderly patients (see also section 5.2).

Renal impairment

No dose adjustment is required in patients with renal impairment (see section 5.2). Serum calcium should be monitored in patients with severe renal impairment or receiving dialysis (see section 4.4).

Hepatic impairment

No clinical trials have been conducted to evaluate the effect of hepatic impairment (see section 5.2).

Paediatric population

The safety and efficacy of romosozumab in paediatric patients (age <18 years) have not yet been established. No data are available.

Method of administration

Subcutaneous use

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.

Administration should be performed by an individual who has been trained in injection techniques.

For instructions on handling and disposal see section 6.6.

4.3 Contraindications

- Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1 (see section 4.4)
- Hypocalcaemia (see section 4.4)
- History of myocardial infarction or stroke (see section 4.4)

4.4 Special warnings and precautions for use

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 (see section 4.8).

Romosozumab is contraindicated in patients with previous myocardial infarction or stroke (see section 4.3).

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 prescriber and patient agree that the benefit outweighs the risk. If a patient experiences a myocardial infarction or stroke during therapy, treatment with romosozumab should be discontinued.

Hypocalcaemia

Transient hypocalcaemia has been observed in patients receiving romosozumab.

Hypocalcaemia should be corrected prior to initiating therapy with romosozumab and patients should be monitored for signs and symptoms of hypocalcaemia. If any patient presents with suspected symptoms of hypocalcaemia during treatment (see section 4.8), calcium levels should be measured. Patients should be adequately supplemented with calcium and vitamin D (see sections 4.3 and 4.8).

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 hypocalcaemia and the safety data for these patients is limited. Calcium levels should be monitored in these patients.

Hypersensitivity

Clinically significant hypersensitivity reactions, including angioedema, erythema multiforme, and urticaria occurred in the romosozumab group in clinical trials. If an anaphylactic or other clinically significant allergic reaction occurs, appropriate therapy should be initiated and use of romosozumab should be discontinued (see sections 4.3 and 4.8).

Osteonecrosis of the jaw

Osteonecrosis of the jaw (ONJ), has been reported rarely in patients receiving romosozumab. The following risk factors should be considered when evaluating a patient's risk of developing ONJ:

- 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 head and neck.
- poor oral hygiene, periodontal disease, poorly fitting dentures, history of dental disease, invasive dental procedures e.g. tooth extractions.

All patients should be encouraged to maintain good oral hygiene, receive routine dental check-ups, and immediately report any oral symptoms such as dental mobility, pain or swelling or non-healing of sores or discharge during treatment with romosozumab.

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.

Atypical femoral fractures

Atypical low-energy or low trauma fracture of the femoral shaft, which can occur spontaneously, has been reported rarely in patients receiving romosozumab. Any patient who presents with new or unusual thigh, hip, 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 romosozumab therapy should be considered, based on an individual 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.

4.5 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.

4.6 Fertility, pregnancy and lactation

Pregnancy

Romozumab is not indicated for use in women of child-bearing potential or in pregnant women. There are no data from the use of romozumab in pregnant women. Skeletal malformations (including syndactyly and polydactyly) were observed at a low incidence in a single study with romozumab in rats (see section 5.3). A risk for malformations of developing digits in the human foetus is low following romozumab exposure due to the timing of digit formation in the first trimester in humans, a period when placental transfer of immunoglobulins is limited.

Breast-feeding

Romozumab is not indicated for use in breast-feeding women.

No data are available on excretion of romozumab in human milk. Human IgGs are known to be excreted in breast milk during the first few days after birth, which is decreasing to low concentrations soon afterwards; consequently, a risk to the breast-fed infant cannot be excluded during this short period.

Fertility

No data are available on the effect of romozumab on human fertility. Animal studies in female and male rats did not show any effects on fertility endpoints (see section 5.3).

4.7 Effects on ability to drive and use machines

Romozumab has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Summary of the safety profile

The most common adverse reactions were nasopharyngitis (13.6%) and arthralgia (12.4%). Hypersensitivity-related reactions occurred in 6.7% of patients treated with romozumab. Hypocalcaemia was reported uncommonly (0.4% of patients treated with romozumab). In randomised controlled studies, an increase in serious cardiovascular events (myocardial infarction and stroke) has been observed in romozumab treated patients compared to controls (see section 4.4 and information below).

Tabulated list of adverse reactions

The following convention has been used for the classification of the adverse reactions: very common ($\geq 1/10$), common ($\geq 1/100$ to $< 1/10$), uncommon ($\geq 1/1,000$ to $< 1/100$), rare ($\geq 1/10,000$ to $< 1/1,000$) and very rare ($< 1/10,000$). Within each frequency grouping and system organ class, adverse reactions are presented in order of decreasing seriousness.

MedDRA System Organ Class	Adverse reaction	Frequency category
<i>Infections and infestations</i>	Nasopharyngitis Sinusitis	Very common Common
<i>Immune system disorders</i>	Hypersensitivity ^a Rash Dermatitis Urticaria Angioedema Erythema multiforme	Common Common Common Uncommon Rare Rare
<i>Metabolism and nutrition disorders</i>	Hypocalcaemia ^b	Uncommon
<i>Nervous system disorders</i>	Headache Stroke ^c	Common Uncommon
<i>Eye disorders</i>	Cataract	Uncommon
<i>Cardiac disorders</i>	Myocardial infarction ^c	Uncommon
<i>Musculoskeletal and connective tissue disorders</i>	Arthralgia Neck pain Muscle spasms	Very common Common Common
<i>General disorders and administration site conditions</i>	Injection site reactions ^d	Common

a. See sections 4.3 and 4.4.

b. Defined as albumin adjusted serum calcium that was below the lower limit of normal. See sections 4.3 and 4.4.

c. See section "Myocardial infarction and stroke" below.

d. Most frequent injection site reactions were pain and erythema.

Description of selected adverse reactions

Immunogenicity

In postmenopausal women dosed with monthly romosozumab, the incidence of anti-romosozumab antibodies was 18.6% (1162 of 6244) for binding antibodies and 0.9% (58 of 6244) for neutralizing antibodies. The earliest onset of anti-romosozumab antibodies was 3 months after first dosing. The majority of antibody responses were transient.

The presence of anti-romosozumab binding antibodies decreased romosozumab exposure by up to 25%. No impact on the efficacy of romosozumab was observed in the presence of antiromosozumab antibodies. Limited safety data show that the incidence of injection site reactions was numerically higher in female patients with neutralizing antibodies.

Myocardial infarction, stroke and mortality

In the active-controlled trial of romosozumab for the treatment of severe osteoporosis in postmenopausal women during the 12-month double-blind romosozumab treatment phase, 16 women (0.8%) had myocardial infarction in the romosozumab arm versus 5 women (0.2%) in the alendronate arm and 13 women (0.6%) had stroke in the romosozumab arm versus 7 women (0.3%) in the alendronate arm. 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 romosozumab group and 12 (0.6%) women in the alendronate group. The number of women with major adverse cardiac events (MACE = positively adjudicated cardiovascular death, myocardial infarction or stroke) was 41 (2.0%) in the romosozumab group and 22 (1.1%) in the alendronate group, yielding a hazard ratio of 1.87 (95% confidence interval [1.11, 3.14]) for romosozumab compared to alendronate. All-cause death occurred in 30 women (1.5%) in the romosozumab group and 22 (1.1%) women in the alendronate group.

In the placebo-controlled trial of romosozumab for the treatment of osteoporosis in postmenopausal women (including women with severe and less severe osteoporosis) during the 12-month double-blind romosozumab treatment phase, there was no difference in positively adjudicated MACE; 30 (0.8%)

occurred in the romosozumab group and 29 (0.8%) in the placebo group. All-cause death occurred in 29 women (0.8%) in the romosozumab group and 24 (0.7%) women in the placebo group.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via **the national reporting system** listed in [Appendix V](#).

4.9 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.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Medicinal products for treatment of bone diseases, medicinal products affecting bone structure and mineralization, ATC code: M05BX06.

Mechanism of action

Romosozumab is a humanized monoclonal antibody (IgG2) that binds and inhibits sclerostin, thereby increasing bone formation due to the activation of bone lining cells, increasing bone matrix production by osteoblasts, and recruitment of osteoprogenitor cells. Additionally, romosozumab results in changes to expression of osteoclast mediators, thereby decreasing bone resorption. Together, this dual effect of increasing bone formation and decreasing bone resorption results in rapid increases in trabecular and cortical bone mass, improvements in bone structure, and strength.

Pharmacodynamic effects

In postmenopausal women with osteoporosis, romosozumab increased the bone formation marker procollagen Type 1 N terminal propeptide (P1NP) early in treatment, with a peak increase of approximately 145% relative to placebo 2 weeks after initiating treatment, followed by a return to placebo levels at month 9 and a decline to approximately 15% below placebo at month 12. Romosozumab decreased the bone resorption marker type-1 collagen C-telopeptide (CTX) with a maximal reduction of approximately 55% relative to placebo 2 weeks after initiating treatment. CTX levels remained below placebo and were approximately 25% below placebo at month 12.

After discontinuation of romosozumab therapy in postmenopausal women with osteoporosis, P1NP levels returned to baseline within 12 months; CTX increased above baseline levels within 3 months and returned toward baseline levels by month 12, reflecting reversibility of effect. Upon retreatment with romosozumab (in a limited number of patients) after 12 months placebo treatment, the levels of increase in P1NP and decrease in CTX by romosozumab were similar to that observed during the initial treatment.

Clinical trial efficacy

Treatment of osteoporosis in postmenopausal women

Efficacy and safety of romosozumab was assessed in two pivotal studies, an alendronate-controlled (ARCH) and a placebo-controlled study (FRAME).

Study 20110142 (ARCH)

The efficacy and safety of romosozumab in the treatment of osteoporosis in postmenopausal women was evaluated in a multicenter, multinational, randomized, double-blind, alendronate-controlled, superiority study of 4,093 postmenopausal women aged 55 to 90 years (mean age of 74.3 years) with previous fragility fractures.

Enrolled women had either a BMD (Bone Mineral Density) T-score at the total hip or femoral neck of ≤ -2.50 , and either at least 1 moderate or severe vertebral fracture; or at least 2 mild vertebral fractures; or a BMD T-score at the total hip or femoral neck of ≤ -2.00 , and either at least 2 moderate or severe vertebral fractures; or a fracture of the proximal femur that occurred within 3 to 24 months prior to randomization.

The mean baseline lumbar spine, total hip, and femoral neck BMD T-scores were -2.96, -2.80, and -2.90, respectively, 96.1% of women had a vertebral fracture at baseline, and 99.0% of women had a previous osteoporotic fracture. Women were randomized (1:1) to receive either monthly subcutaneous injections of romosozumab or oral weekly alendronate in a blinded fashion for 12 months. After the 12-month double blind study period, women in both arms transitioned to alendronate while remaining blinded to their initial treatment. The primary analysis was performed when all women had completed the month 24 study visit and clinical fracture events were confirmed for at least 330 women and occurred after a median follow-up time of approximately 33 months on study. Women received calcium and vitamin D supplementation daily.

The primary efficacy endpoints were the incidence of new vertebral fracture through month 24 and the incidence of clinical fracture (nonvertebral fracture and clinical vertebral fracture) at primary analysis.

Effect on new vertebral, clinical, nonvertebral, hip and major osteoporotic fractures

As shown in Table 1, romosozumab reduced the incidence of new vertebral fracture through month 24 (adjusted p-value < 0.001) and the incidence of clinical fracture at primary analysis (adjusted p-value < 0.001) as well as the incidence of non vertebral fractures at primary analysis (adjusted p-value = 0.040) versus treatment with alendronate alone. Table 1 also shows nonvertebral, hip and major osteoporotic fracture risk reduction through primary analysis, month 12 and month 24.

Table 1. The Effect of romosozumab on the incidence and risk of new Vertebral, clinical, nonvertebral, hip and major osteoporotic fractures in post-menopausal women with osteoporosis

	Proportion of women with fracture		Absolute risk reduction (%) (95% CI)	Relative risk reduction (%) (95% CI)
	Alendronate/Alendronate (%)	Romosozumab/Alendronate (%)		
<i>New vertebral</i>				
Through month 12	85/1703 (5.0)	55/1696 (3.2)	1.84 (0.51, 3.17)	36 (11, 54)
Through month 24 ^a	147/1834 (8.0)	74/1825 (4.1)	4.03 (2.50, 5.57)	50 (34, 62)
<i>Clinical^b</i>				
Through month 12	110/2047 (5.4)	79/2046 (3.9)	1.8 (0.5, 3.1)	28 (4, 46)
Primary analysis (median follow-up approx. 33 months)	266/2047 (13.0)	198/2046 (9.7)	NA ^c	27 (12, 39)
<i>Nonvertebral</i>				
Through Month 12	95/2047 (4.6)	70/2046 (3.4)	1.4 (0.1, 2.6)	26 (-1, 46)
Primary analysis (median follow-up approx. 33 months)	217/2047 (10.6)	178/2046 (8.7)	NA ^c	19 (1, 34)
<i>Hip</i>				
Through Month 12	22/2047 (1.1)	14/2046 (0.7)	0.3 (-0.3, 0.9)	36 (-26, 67)
Primary analysis (median follow-up approx. 33 months)	66/2047 (3.2)	41/2046 (2.0)	NA ^c	38 (8, 58)
<i>Major osteoporotic^d</i>				
Through Month 12	85/2047 (4.2)	61/2046 (3.0)	1.4 (0.3, 2.5)	28 (-1, 48)
Primary analysis (median follow-up approx. 33 months)	209/2047 (10.2)	146/2046 (7.1)	NA ^c	32 (16, 45)

a. Absolute risk reduction and relative risk reduction based on Mantel-Haenszel method adjusted for age strata, baseline total hip BMD T-score (≤ -2.5 , > -2.5), and presence of severe vertebral fracture at baseline. Treatment comparisons are based on adjusted logistic regression model.

b. Clinical fractures include all symptomatic fractures including nonvertebral and painful vertebral fractures. Treatment comparisons are based on Cox proportional hazards model.

c. NA: not available as subjects have various exposure at primary analysis.

d. Major osteoporotic fractures include hip, forearm, humerus, and clinical vertebral.

Effect on Bone Mineral Density (BMD)

In postmenopausal women with osteoporosis, romosozumab for 12 months followed by alendronate for 12 months increased BMD compared with alendronate alone at month 12 and 24 (p-value < 0.001) (see Table 2).

Following 12 months of treatment, romosozumab increased BMD at the lumbar spine from baseline in 98% of postmenopausal women.

Table 2. Mean percent change in BMD from baseline through month 12 and month 24 in postmenopausal women with osteoporosis

	Alendronate/Alendronate Mean (95% CI) N = 2047^a	Romosozumab/Alendronate Mean (95% CI) N = 2046^a	Treatment difference from alendronate-to- alendronate
<i>At Month 12</i>			
Lumbar spine	5.0 (4.8, 5.2)	12.4 (12.1, 12.7)	7.4 ^b (7.0, 7.8)
Total hip	2.9 (2.7, 3.1)	5.8 (5.6, 6.1)	2.9 ^b (2.7, 3.2)
Femoral neck	2.0 (1.8, 2.2)	4.9 (4.6, 5.1)	2.8 ^b (2.5, 3.2)
<i>At Month 24</i>			
Lumbar spine	7.2 (6.9, 7.5)	14.0 (13.6, 14.4)	6.8 ^b (6.4, 7.3)
Total hip	3.5 (3.3, 3.7)	6.7 (6.4, 6.9)	3.2 ^b (2.9, 3.6)
Femoral neck	2.5 (2.3, 2.8)	5.7 (5.4, 6.0)	3.2 ^b (2.8, 3.5)

Means and confidence intervals are based on patients with available data. Based on ANCOVA model; missing values of baseline BMD and BMD percent change from baseline at month 12 and month 24 were imputed by control-based pattern imputation.

a. Number of women randomized

b. p-value < 0.001

The significant difference in BMD achieved in the first 12 months was maintained through month 36 upon transition/continuation to alendronate. Treatment differences were observed at 6 months at lumbar spine, total hip and femoral neck.

Study 20070337 (FRAME)

The efficacy and safety of romosozumab in the treatment of postmenopausal osteoporosis was evaluated in a multicenter, multinational, randomized, double-blind, placebo-controlled, parallel-group study of 7,180 postmenopausal women aged 55 to 90 years (mean age of 70.9 years). 40.8% of enrolled women had severe osteoporosis with a prior fracture at baseline.

The co-primary efficacy endpoints were the incidence of new vertebral fractures through month 12 and through month 24.

Romosozumab reduced the incidence of new vertebral fractures through month 12 (absolute risk reduction: 1.3% [95% CI: 0.79; 1.80], relative risk reduction: 73% [95% CI: 53; 84], adjusted p-value < 0.001) and after transition to denosumab through month 24 (absolute risk reduction: 1.89% [95% CI: 1.30; 2.49], relative risk reduction: 75% [95% CI: 60, 84], adjusted p-value < 0.001).

Women transitioning from bisphosphonate therapy

Study 20080289 (STRUCTURE)

The safety and efficacy of romosozumab in postmenopausal women with severe osteoporosis transitioning from bisphosphonate therapy (92.7% in teriparatide group and 88.1% in romosozumab group had prior alendronate use during the last 3 years) were evaluated in a multicenter, randomized, open-label study of 436 postmenopausal women aged 56 to 90 years (mean age of 71.5 years) versus teriparatide.

The primary efficacy variable was percent change in total hip BMD from baseline at month 12. Romosozumab significantly increased BMD at the total hip relative to teriparatide at month 12 (mean treatment difference from Teriparatide: 3.4% [95% CI: 2.8; 4.0], p-value < 0.0001). The trial was not intended to estimate the effect on fractures but there were seven fractures in the romosozumab arm and nine fractures in the teriparatide arm of the study.

Bone Histology and Histomorphometry

In a bone histology sub-study, a total of 154 transiliac crest bone biopsy specimens were obtained from 139 postmenopausal women with osteoporosis at months 2 and 12 (in FRAME study). Qualitative histology assessments showed normal bone architecture and quality at all time points, normal lamellar bone with no evidence of mineralization defects, woven bone, marrow fibrosis, or clinically significant marrow abnormality in patients treated with romosozumab.

Histomorphometry assessments on biopsies at months 2 and 12 in women showed an increase of bone formation parameters and a decrease in bone resorption parameters while bone volume and trabecular thickness were increased in romosozumab group compared to placebo group.

Paediatric population

The European Medicines Agency has deferred the obligation to submit the results of studies with romosozumab in one or more subsets of the paediatric population in the treatment of osteoporosis. See section 4.2 for information on paediatric use.

5.2 Pharmacokinetic properties

Absorption

The median time to maximum romosozumab concentration (t_{max}) was 5 days (range: 2 to 7 days). Following a 210 mg subcutaneous dose, bioavailability was 81%.

Biotransformation

Romosozumab is a humanized monoclonal antibody (IgG2) with high affinity and specificity for sclerostin, and therefore is cleared via a rapid saturable elimination pathway (i.e. target mediated nonlinear clearance, mediated by degradation of the romosozumab-sclerostin complex) and via a slow nonspecific elimination pathway mediated by the reticuloendothelial system.

Elimination

After C_{max} , serum levels declined with a mean effective half-life of 12.8 days. Steady-state was generally reached by month 3 with less than 2-fold accumulation following monthly dosing.

Linearity/non-linearity

Following subcutaneous administration, romosozumab exhibits non-linear pharmacokinetics as a result of binding to sclerostin. Multiple doses administered ranged from 70 to 210 mg.

Renal impairment

Following a 210 mg dose of romosozumab in a clinical trial of 16 patients with severe renal impairment (creatinine clearance < 30 ml/min) or end-stage renal disease (ESRD) receiving haemodialysis, mean C_{max} and AUC were 29% and 44% higher in patients with severe renal impairment as compared to healthy subjects. Mean romosozumab exposure was similar in patients with ESRD receiving haemodialysis as compared to healthy subjects.

Population pharmacokinetic analysis indicated an increase in romosozumab exposure with increasing severity of renal impairment. However, based on an exposure-response model of BMD changes and comparison to exposures obtained at tolerated clinical doses, no dose adjustment is recommended in these patients. Monitoring of hypocalcemia in patients with severe renal impairment or receiving dialysis is recommended (see section 4.4).

Hepatic impairment

No clinical trials have been conducted to evaluate the effect of hepatic impairment. Hepatic impairment is not expected to impact on the pharmacokinetics of romosozumab since the liver is not a major organ for romosozumab metabolism or excretion.

Elderly

The pharmacokinetics of romosozumab were not affected by age from 20 years to 89 years.

Bodyweight

Romosozumab exposure decreased with increasing body weight however this decrease had a minimal impact on lumbar spine BMD gain based on exposure-response analysis and is not clinically meaningful. Based on population PK analyses, the expected median steady state AUC for a 61 kg and 114 kg patient is 558 µg.day/ml and 276 µg.day/ml respectively following a monthly subcutaneous dose of 210 mg romosozumab.

Ethnicity and gender

No dose adjustment is necessary for any patient characteristics. Based on a population pharmacokinetic analysis, gender and race (Japanese versus non-Japanese) had no clinically meaningful impact on the pharmacokinetics of romosozumab (< 20% change in exposure at steady state).

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, carcinogenic potential or in bone safety studies.

In a carcinogenicity study, doses up to 50 mg/kg/week were administered by subcutaneous injection to Sprague-Dawley male and female rats from 8 weeks of age for up to 98 weeks. These doses resulted in systemic exposures that were up to 19 times higher than the systemic exposure observed in humans following a monthly subcutaneous dose of 210 mg romosozumab (based on AUC comparison). Romosozumab caused a dose-dependent increase in bone mass with macroscopic bone thickening at all doses. There were no effects of romosozumab on mortality or tumor incidence in male or female rats.

Studies in female and male rats did not show any romosozumab-related effects on mating, fertility, or male reproductive assessments (sperm parameters or organ weights), and there were no effects on estrous cycling or any ovarian or uterine parameters at exposures around 54 times the clinical exposure.

Skeletal malformations, including syndactyly and polydactyly, were observed at a low incidence in 1 out of 75 litters at exposures around 30 times the clinical exposure following administration of romosozumab to rats during the period of organogenesis. There were no adverse effects on postnatal growth and development.

Sclerostin has been suggested to have a role in digit formation, however, as digit formation in the human occurs in the first trimester when placental transfer of immunoglobulins is limited, the risk of a similar finding in humans is low (see section 4.6).

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Calcium acetate
Glacial acetic acid
Sodium hydroxide (for pH adjustment)
Sucrose
Polysorbate 20
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

3 years.

When taken out of the refrigerator for use, EVENITY should not be returned to the refrigerator but can be kept at room temperature (up to 25°C) for up to 30 days in the original container. If not used within this period, the product should be discarded.

6.4 Special precautions for storage

Store in a refrigerator (2°C - 8°C). Do not freeze.
Keep the pre-filled syringe or pre-filled pen in the outer carton in order to protect from light.

6.5 Nature and contents of container

EVENITY 105 mg solution for injection in pre-filled pen

A single use, disposable, handheld, mechanical injection device pre-assembled with pre-filled syringe containing 1.17 ml solution. The syringe inside the pen is made from cyclo olefin polymer plastic with a stopper (chlorobutyl) and insert molded stainless steel needle with elastomeric needle shield (synthetic rubber).

Pack size of 2 pre-filled pens.
Multipack containing 6 (3 packs of 2) pre-filled pens.

EVENITY 105 mg solution for injection in pre-filled syringe

A single use, disposable, pre-filled syringe containing 1.17 ml solution. The syringe is made from cyclo olefin polymer plastic with a stopper (chlorobutyl) and insert molded stainless steel needle and elastomeric needle shield (synthetic rubber).

Pack size of 2 pre-filled syringes.
Multipack containing 6 (3 packs of 2) pre-filled syringes.

Not all pack sizes may be marketed.

6.6 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.

Prior to subcutaneous administration, romosozumab should be allowed to sit at room temperature for at least 30 minutes before injecting. This will help make the injection more comfortable. It should not be warmed in any other way.

Do not shake.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

UCB Pharma S.A.
Allée de la Recherche, 60
B-1070 Bruxelles
Belgium

8. MARKETING AUTHORISATION NUMBER(S)

EU/1/19/1411/001
EU/1/19/1411/002
EU/1/19/1411/003
EU/1/19/1411/004

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

Detailed information on this medicinal product is available on the website of the European Medicines Agency <http://www.ema.europa.eu>

ANNEX II

- A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE**
- B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE**
- C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION**
- D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT**

A. MANUFACTURER OF THE BIOLOGICAL ACTIVE SUBSTANCE AND MANUFACTURER RESPONSIBLE FOR BATCH RELEASE

Name and address of the manufacturer of the biological active substance

Immunex Rhode Island Corporation
40 Technology Way, West Greenwich
Rhode Island 02817
United States

Name and address of the manufacturer responsible for batch release

Amgen Europe B.V.
Minervum 7061
NL-4817 ZK Breda
NETHERLANDS

B. CONDITIONS OR RESTRICTIONS REGARDING SUPPLY AND USE

Medicinal product subject to restricted medical prescription (see Annex I: Summary of Product Characteristics, section 4.2).

C. OTHER CONDITIONS AND REQUIREMENTS OF THE MARKETING AUTHORISATION

- **Periodic safety update reports**

The requirements for submission of periodic safety update reports for this medicinal product are set out in the list of Union reference dates (EURD list) provided for under Article 107c(7) of Directive 2001/83/EC and any subsequent updates published on the European medicines web-portal.

The marketing authorisation holder shall submit the first periodic safety update report for this product within 6 months following authorisation.

D. CONDITIONS OR RESTRICTIONS WITH REGARD TO THE SAFE AND EFFECTIVE USE OF THE MEDICINAL PRODUCT

- **Risk Management Plan (RMP)**

The MAH shall perform the required pharmacovigilance activities and interventions detailed in the agreed RMP presented in Module 1.8.2 of the marketing authorisation and any agreed subsequent updates of the RMP.

An updated RMP should be submitted:

- At the request of the European Medicines Agency;
- Whenever the risk management system is modified, especially as the result of new information being received that may lead to a significant change to the benefit/risk profile or as the result of an important (pharmacovigilance or risk minimisation) milestone being reached.

- **Additional risk minimisation measures**

The MAH shall ensure that the educational programme is implemented for the authorised indications of treatment of severe osteoporosis in postmenopausal women at high risk of fracture.

The educational program is aimed at further minimizing the risks of serious cardiovascular events of myocardial infarction (MI) and stroke, hypocalcaemia, and of osteonecrosis of the jaw (ONJ) by reinforcing the key safety information available in the SmPC and the PIL.

The educational programme contains the following:

- Physician educational material
- Patient alert card

The **physician educational material** should contain the following key elements:

- The Summary of Product Characteristics
- Prescriber Guide:
 - Relevant information to support healthcare professionals (HCPs) in the appropriate recognition, monitoring and management of the important identified risks of serious cardiovascular (CV) events of MI and stroke and of hypocalcaemia and important potential risk of ONJ.
 - A reminder list of risk minimization actions to be performed prior to prescription of romosozumab.
 - A checklist, which reminds the prescriber to verify the contraindication and perform a careful assessment of the cardiovascular risk profile before prescribing romosozumab.
 - Instruction for a prompt medical evaluation for patients who develop symptoms suggestive of MI or stroke, which will enable a rapid re-assessment of the benefit-risk, leading to the appropriate actions regarding romosozumab treatment.
 - A reminder to the healthcare professional to educate the patient and/or caregiver on the risks, especially on the CV risk, and ensure the patient is provided with a Patient Alert Card.
 - Reminding need for and how to report suspected adverse reactions.

The **patient alert card** should be provided and contain the following key messages:

- Signs and/or symptoms of the safety concerns of serious cardiovascular events of MI and stroke, hypocalcaemia, and ONJ and when to seek attention from a healthcare professional.
- Providing a reminder to the patient/caregiver to share information on history of MI or stroke and other CV conditions/risk factors to the osteoporosis specialist.
- The importance of carrying the Patient Alert Card at all times and showing it to all healthcare professionals.
- Administration dates of romosozumab and contact details of the prescribing physician to be contacted for advice if needed.
- Important information for other healthcare professionals relevant to the patient taking romosozumab, including for the important identified risks of serious cardiovascular events of MI and stroke and of hypocalcaemia and important potential risk of ONJ.
- Reminding the need to report side effects by patients, caregivers, or any other HCP.

ANNEX III
LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED PEN CARTON

1. NAME OF THE MEDICINAL PRODUCT

EVENTITY 105 mg solution for injection in pre-filled pen
romosozumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled pen contains 105 mg of romosozumab in 1.17 ml of solution (90mg/ml).

3. LIST OF EXCIPIENTS

Excipients: calcium acetate, glacial acetic acid, sodium hydroxide, sucrose, polysorbate 20 and water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
2 single-use pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For subcutaneous use.
Read the package leaflet before use.
Do not shake.

Picture on the front of the carton:



Picture and text inside the box, visible upon opening:

To receive full dose, take two.
Read the package leaflet before use.



6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Keep the pen in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

UCB Pharma S.A. (logo)
Allée de la Recherche 60
B-1070 Bruxelles
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/19/1411/001
EU/1/19/1411/002
EU/1/19/1411/003
EU/1/19/1411/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

EVENTY 105 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:

SN:

NN:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON OF MULTIPACK (WITH BLUEBOX)

1. NAME OF THE MEDICINAL PRODUCT

EVENTY105 mg solution for injection in pre-filled pen
romosozumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled pen contains 105 mg of romosozumab in 1.17 ml of solution (90mg/ml).

3. LIST OF EXCIPIENTS

Excipients: calcium acetate, glacial acetic acid, sodium hydroxide, sucrose, polysorbate 20 and water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

Multipack: 6 (3 packs of 2) single-use pre-filled pens

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For subcutaneous use.
Read the package leaflet before use.
Do not shake.

Picture on the front of the carton:



6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Keep the pen in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

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B-1070 Bruxelles
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12. MARKETING AUTHORISATION NUMBER(S)

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EU/1/19/1411/002
EU/1/19/1411/003
EU/1/19/1411/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

EVENTY 105 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON WITHIN MULTIPACK (WITHOUT BLUEBOX)

1. NAME OF THE MEDICINAL PRODUCT

EVENTITY 105 mg solution for injection in pre-filled pen
romosozumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled pen contains 105 mg of romosozumab in 1.17 ml of solution (90mg/ml).

3. LIST OF EXCIPIENTS

Excipients: calcium acetate, glacial acetic acid, sodium hydroxide, sucrose, polysorbate 20 and water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection

2 single-use pre-filled pens. Component of a multipack, can't be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For subcutaneous use.
Read the package leaflet before use.
Do not shake.

Picture on the front of the carton:



Picture and text inside the box, visible upon opening:

To receive full dose, take two.
Read the package leaflet before use.



6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.
Do not freeze.
Keep the pen in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

UCB Pharma S.A. (logo)
Allée de la Recherche 60
B-1070 Bruxelles
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

EU/1/19/1411/001
EU/1/19/1411/002
EU/1/19/1411/003
EU/1/19/1411/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

EVENTY 105 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
PRE-FILLED PEN LABEL**

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

EVENTITY 105 mg injection
romosozumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1.17 ml

6. OTHER

UCB Pharma S.A. (logo)

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

PRE-FILLED SYRINGE CARTON

1. NAME OF THE MEDICINAL PRODUCT

EVENTITY 105 mg solution for injection in pre-filled syringe
romosozumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled syringe contains 105 mg of romosozumab in 1.17 ml of solution (90mg/ml).

3. LIST OF EXCIPIENTS

Excipients: calcium acetate, glacial acetic acid, sodium hydroxide, sucrose, polysorbate 20 and water for injections

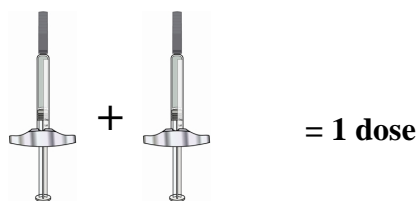
4. PHARMACEUTICAL FORM AND CONTENTS

Solution for injection
2 single-use pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For subcutaneous use.
Read the package leaflet before use.
Do not shake.

Picture on the front of the carton:



6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

Do not freeze.

Keep the pre-filled syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

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Allée de la Recherche 60
B-1070 Bruxelles
Belgium

12. MARKETING AUTHORISATION NUMBER(S)

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EU/1/19/1411/002
EU/1/19/1411/003
EU/1/19/1411/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

EVENTY 105 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

OUTER CARTON OF MULTIPACK (WITH BLUEBOX)

1. NAME OF THE MEDICINAL PRODUCT

EVENTITY 105 mg solution for injection in pre-filled syringe
romosozumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled syringe contains 105 mg of romosozumab in 1.17 ml of solution (90 mg/ml).

3. LIST OF EXCIPIENTS

Excipients: calcium acetate, glacial acetic acid, sodium hydroxide, sucrose, polysorbate 20 and water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

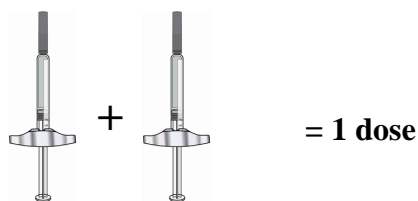
Solution for injection

Multipack: 6 (3 packs of 2) single-use pre-filled syringes

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For subcutaneous use.
Read the package leaflet before use.
Do not shake.

Picture on the front of the carton:



6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

Do not freeze.

Keep the syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

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B-1070 Bruxelles
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12. MARKETING AUTHORISATION NUMBER(S)

EU/1/19/1411/001
EU/1/19/1411/002
EU/1/19/1411/003
EU/1/19/1411/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

EVENITY 105 mg

17. UNIQUE IDENTIFIER – 2D BARCODE

2D barcode carrying the unique identifier included.

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

PC:
SN:
NN:

PARTICULARS TO APPEAR ON THE OUTER PACKAGING

INTERMEDIATE CARTON WITHIN MULTIPACK (WITHOUT BLUEBOX)

1. NAME OF THE MEDICINAL PRODUCT

EVENTITY 105 mg solution for injection in pre-filled syringe
romosozumab

2. STATEMENT OF ACTIVE SUBSTANCE(S)

Each pre-filled syringe contains 105 mg of romosozumab in 1.17 ml of solution (90 mg/ml)..

3. LIST OF EXCIPIENTS

Excipients: calcium acetate, glacial acetic acid, sodium hydroxide, sucrose, polysorbate 20 and water for injections

4. PHARMACEUTICAL FORM AND CONTENTS

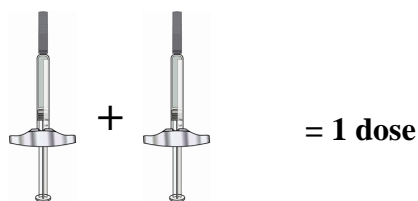
Solution for injection

2 single-use pre-filled syringes. Component of a multipack, can't be sold separately.

5. METHOD AND ROUTE(S) OF ADMINISTRATION

For subcutaneous use.
Read the package leaflet before use.
Do not shake.

Picture on the front of the carton:



6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

8. EXPIRY DATE

EXP

9. SPECIAL STORAGE CONDITIONS

Store in a refrigerator.

Do not freeze.

Keep the syringe in the outer carton in order to protect from light.

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE**11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER**

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12. MARKETING AUTHORISATION NUMBER(S)

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EU/1/19/1411/003
EU/1/19/1411/004

13. BATCH NUMBER

Lot

14. GENERAL CLASSIFICATION FOR SUPPLY**15. INSTRUCTIONS ON USE****16. INFORMATION IN BRAILLE**

EVENITY 105 mg

17. UNIQUE IDENTIFIER – 2D BARCODE**18. UNIQUE IDENTIFIER - HUMAN READABLE DATA**

**MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS
PRE-FILLED SYRINGE LABEL**

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

EVENTITY 105 mg injection
romosozumab
SC

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

EXP

4. BATCH NUMBER

Lot

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

1.17 ml

6. OTHER

UCB Pharma S.A. (logo)

B. PACKAGE LEAFLET

Package leaflet: Information for the user

EVENTITY 105 mg solution for injection in pre-filled pen romosozumab

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.
- You will be given a patient alert card, which contains important safety information you need to be aware of before and during your treatment with EVENTITY.

What is in this leaflet

1. What EVENTITY is and what it is used for
2. What you need to know before you use EVENTITY
3. How to use EVENTITY
4. Possible side effects
5. How to store EVENTITY
6. Contents of the pack and other information

1. What EVENTITY is and what it is used for

What EVENTITY is

EVENTITY contains the active substance romosozumab, a medicine that helps to make the bones stronger, and reduce the risk of broken bones.

What EVENTITY is used for

EVENTITY is used to treat severe osteoporosis in women after the menopause who are at high risk of broken bone (fracture).

Osteoporosis is a disease that causes your bones to become thin and fragile. Many patients with osteoporosis have no symptoms, but they may be at increased risk of fractures.

How EVENTITY works

EVENTITY is a monoclonal antibody. A monoclonal antibody is a type of protein that has been designed to recognize and attach to specific proteins in the body. EVENTITY attaches to a protein called sclerostin. By attaching to and blocking the activity of sclerostin, EVENTITY:

- helps to form new bone, and
- slows down the loss of existing bone.

This makes the bones stronger, and lowers the risk of fractures.

2. What you need to know before you use EVENITY

Do not use EVENITY if

- you are allergic to romosozumab or any of the other ingredients of this medicine (listed in section 6);
- you have low levels of calcium in the blood (hypocalcaemia). Your doctor will be able to tell you if your levels are too low;
- you have a history of heart attack or stroke.

Do not use EVENITY if any of the above applies to you. If you are not sure, talk to your doctor or pharmacist before using EVENITY.

Warnings and precautions

Talk to your doctor or pharmacist and discuss your medical history before using EVENITY.

Heart attack and stroke

Heart attack and stroke have been reported in people receiving EVENITY.

Seek medical attention straight away if you get:

- chest pain, shortness of breath;
- headache, numbness, or weakness in your face, arms, or legs, difficulty talking, changes in vision, loss of balance.

Your doctor will carefully evaluate the risk of cardiovascular problems before he/she lets you start treatment with EVENITY. Tell your doctor if you know that you have an increased risk of cardiovascular problems such as established cardiovascular disease, high blood pressure, high blood fat levels, diabetes, smoking or kidney problems.

Low levels of calcium in the blood

EVENITY may cause low levels of calcium in your blood.

Tell your doctor if you notice:

- spasms, twitches, or cramps in your muscles;
- numbness or tingling in your fingers, toes or around your mouth.

Your doctor may prescribe calcium and vitamin D to help prevent low calcium levels in your blood before you start your treatment and while you take EVENITY. Take calcium and vitamin D as your doctor tells you to.

Tell your doctor if you have or have ever had severe kidney problems, kidney failure or have needed dialysis as this may increase your risk of getting low blood calcium if you do not take calcium supplements.

Serious allergic reactions

Serious allergic reactions can happen to people who use EVENITY.

Seek medical attention straight away if you get:

- swelling of the face, mouth, throat, hands, feet, ankles, lower legs (angioedema), or hives;
- acute skin eruption showing multiple round, red/pink spots with a blistering or crusting centre (erythema multiforme);
- difficulty in swallowing or breathing.

Problems with your mouth, teeth or jaw

A side effect called osteonecrosis of the jaw (ONJ) (bone damage in the jaw) has been reported rarely (may affect up to 1 in 1,000 people) in patients receiving EVENITY. ONJ can also occur after stopping treatment. It is important to try to prevent ONJ developing, as it may be a painful condition that can be difficult to treat. In order to reduce the risk of developing ONJ, there are some precautions you should take.

Before receiving EVENITY, tell your doctor or nurse if you:

- have any problems with your mouth or teeth such as poor dental health, gum disease, or a planned tooth extraction;
- do not receive routine dental care or have not had a dental check-up for a long time;
- are a smoker (as this may increase the risk of dental problems);
- have previously been treated with a bisphosphonate (used to treat or prevent bone disorders, such as osteoporosis);
- are taking medicines called corticosteroids (such as prednisolone or dexamethasone);
- have cancer.

Your doctor may ask you to undergo a dental examination before you start treatment with EVENITY.

While being treated, you should maintain good oral hygiene and receive routine dental check-ups. If you wear dentures, you should make sure these fit properly. If you are under dental treatment or will undergo dental surgery (e.g. tooth extractions), inform your doctor about your dental treatment and tell your dentist that you are being treated with EVENITY.

Contact your doctor and dentist immediately if you get any problems with your mouth or teeth such as:

- loose teeth;
- pain or swelling;
- mouth sores that do not heal;
- discharge.

Unusual thigh bone fractures

People who have used EVENITY rarely developed unusual fractures of the thigh bone caused by little or no trauma. These fracture types are often preceded by warning signs of thigh or groin pain for several weeks before the fracture occurs. It is not known whether EVENITY caused these unusual fractures. Tell your doctor or pharmacist if you get any new or unusual pains in your hip, groin or thigh.

Children and adolescents

The use of romosozumab in children and adolescents has not been studied and it is not approved for use in paediatric patients (age <18 years).

Other medicines and EVENITY

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Pregnancy and breast-feeding

EVENITY is only intended to treat women after menopause.

EVENITY should not be used by women of child-bearing potential, or when pregnant or breast-feeding. It is not known whether EVENITY may harm an unborn or breast-fed child.

Contact your doctor if you have any questions.

Driving and using machines

EVENITY is expected to have no effect or very little effect on the ability to drive and use machines.

EVENITY contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to use EVENITY

EVENITY will be initiated and supervised by specialist physicians experienced in the management of osteoporosis. Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

The injection should only be given by a person who has been properly trained.

How much to use

- The recommended dose of EVENITY is 210 mg.
- Since one pre-filled pen contains 105 mg of the active substance romosozumab in 1.17 ml of solution (90mg/ml), 2 pre-filled pens must be used for each dose. The second injection must be given immediately after the first one but at a different injection site.
- Do this once every month for 12 months.

How to use

- EVENITY has to be injected under the skin (sub-cutaneous injection).
- EVENITY should be injected in either the stomach area (abdomen) or thigh. The outer area of your upper arm can also be used as an injection site, but only if someone else is giving you the injection.
- If the same injection area is planned to be used for the second injection, a different injection spot should be used.
- EVENITY should not be injected into areas where the skin is tender, bruised, red, or hard.

It is important that you read the **Instructions for Use** for detailed information on how to use the EVENITY pre-filled pen.

Ask your doctor or pharmacist if you have any further questions on the use of the medicine.

If you use more EVENITY than you should

If, by mistake, you have used more EVENITY than you should, contact your doctor or pharmacist.

If you forget to use or cannot take EVENITY at your usual time

If you miss a dose of EVENITY, contact your doctor as soon as possible to schedule another dose. Thereafter, the next dose should be given not earlier than one month after the date of the last dose.

If you stop taking EVENITY

If you are considering stopping EVENITY treatment, please discuss this with your doctor. Your doctor will advise you on how long you should be treated with EVENITY.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

Discuss with your doctor the need to switch to another osteoporosis treatment after the end of your treatment with EVENITY.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Seek medical attention straight away if you get any of the following possible symptoms of **heart attack** or **stroke** (uncommon: may affect up to 1 in 100 people):

- chest pain, shortness of breath;
- headache, numbness, or weakness in your face, arms, or legs, difficulty talking, changes in vision, loss of balance.

Seek medical attention straight away if you get the following symptoms of a **serious allergic reaction** (rare: may affect up to 1 in 1,000 people):

- swelling of the face, mouth, throat, hands, feet, ankles, lower legs (angioedema), or hives;
- acute skin eruption showing multiple round, red/pink spots with a blistering or crusting centre (erythema multiforme);
- difficulty in swallowing or breathing.

Tell your doctor if you notice the following symptoms of **low levels of calcium** in the blood (hypocalcaemia) (uncommon: may affect up to 1 in 100 people):

- spasms, twitches, or cramps in your muscles;
- numbness or tingling in your fingers, toes or around your mouth.

See also section 2 “What you need to know before you use EVENITY”.

Other side effects may include:

Very common side effects (may affect more than 1 in 10 people):

- Common cold;
- Joint pain.

Common side effects (may affect up to 1 in 10 people):

- Rash, inflammation of the skin;
- Headache;
- Sinusitis;
- Neck pain;
- Muscle spasms;
- Redness or pain around the site where the injection was given.

Uncommon side effects (may affect up to 1 in 100 people):

- Hives (urticaria);
- Cataract.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via [the national reporting system listed in Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store EVENITY

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and carton after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C - 8°C). Do not freeze.

Once you take the carton containing the pre-filled pens out of the refrigerator for use, you should not put it back into the refrigerator but you can keep it at room temperature (up to 25°C) for up to 30 days. If not used within this period the product should be discarded.

Keep the pre-filled pen in the outer carton in order to protect from light.

Visually check the solution. Do not use it if the solution is discoloured, cloudy, or contains flakes or particles.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What EVENITY contains

- The active substance is romosozumab. Each pre-filled pen contains 105 mg of romosozumab in 1.17 ml of solution (90mg/ml).
- The other ingredients are calcium acetate, glacial acetic acid, sodium hydroxide (for pH adjustment), sucrose, polysorbate 20 and water for injections. See section 2 “EVENITY contains sodium”

What EVENITY looks like and contents of the pack

EVENITY is a clear to opalescent, colourless to light yellow solution for injection provided in a single use disposable pre-filled pen. The syringe inside the pen is made of plastic with a stainless steel needle.

Pack size of 2 pre-filled pens.

Multipack containing 6 (3 packs of 2) pre-filled pens.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

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Manufacturer

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4817 ZK Breda, Netherlands

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This leaflet was last revised in MM/YYYY.

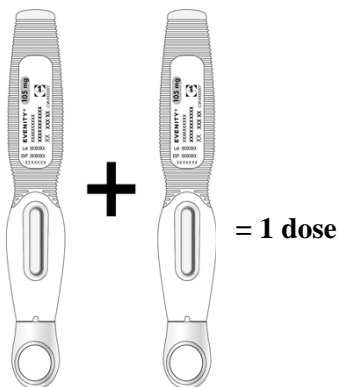
Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu>.

Please turn over for the Instructions for Use.

INSTRUCTIONS FOR USE FOR THE EVENITY INJECTION BY MEANS OF A PRE-FILLED PEN

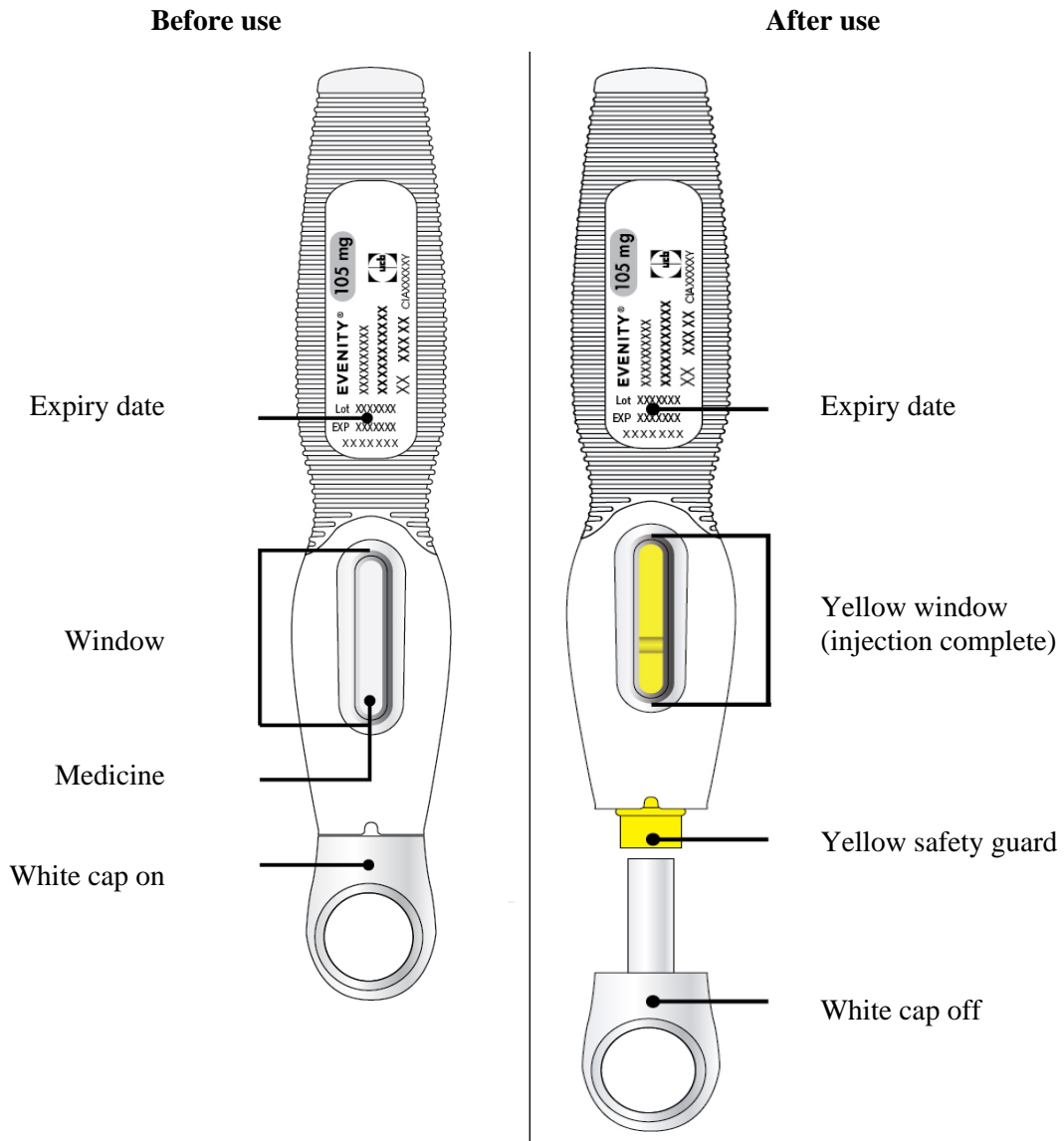
Inject two pre-filled pens one immediately after the other to get a full dose



The following instructions explain how to use the pre-filled pen to inject EVENTITY.

- **Please read these instructions carefully and follow them step by step.**
- If you have any questions or you feel unsure about the injection procedure, please contact a doctor or pharmacist.
- It is important to make sure that the injection is only administered by an individual that has been properly trained.
- The pre-filled pen is also referred to as “the medicine”.

Guide to parts: pre-filled pen

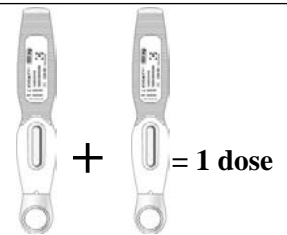


STOP



Read this before the medicine is injected.

Your healthcare provider has prescribed a dose of 210 mg every month: **To receive your full dose, two 105 mg pre-filled pens should be injected, one immediately after the other.**



Step 1: Prepare

- A**
- Take the carton containing the two pre-filled pens out of the refrigerator.
 - Your pre-filled pens should be left outside the refrigerator to reach room temperature (up to 25°C) **for at least 30 minutes** before injection (do not warm in any other way). This will make the injection more comfortable.
 - Open the carton and gather all materials you need for the injection (as listed in Step B).
 - Wash your hands thoroughly.
 - Lift the pre-filled pens straight up out of the carton – do not remove the white caps from the pre-filled pens yet.
 - Do not shake the pre-filled pens.
 - Check the medicine through the viewing window. The medicine should be a clear to opalescent, colourless to light yellow solution.
 - Do not use the pre-filled pens if the solution is discoloured, cloudy, or contains flakes or particles.
 - You may see air bubbles. Injecting the solution subcutaneously (under the skin) which contains air bubbles is harmless.
 - Do not use the pre-filled pens if:
 - it has been dropped;
 - the white cap is missing or not securely attached;
 - the seal is missing or broken or if any other part appears cracked or broken.In such case, use a new pen and contact your doctor as soon as possible.

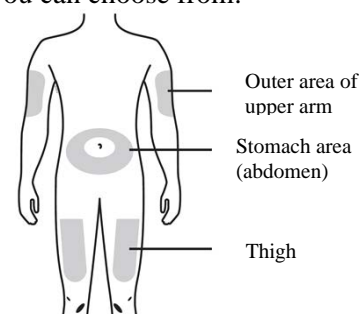
- B** On a clean, well-lit work surface, place:

- two pre-filled pens;
- two alcohol wipes;
- two cotton balls or gauze pads;
- two adhesives bandages;
- special disposal container.

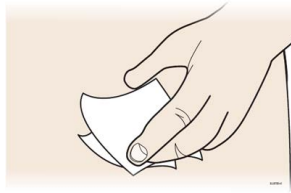


- C** Prepare and clean the skin where you are going to inject the medicine. You can choose from:

- the thighs;
- the stomach area (abdomen), but not the 5 cm area around the belly button;
- the outer area of the upper arm (if someone else is giving you the injection).



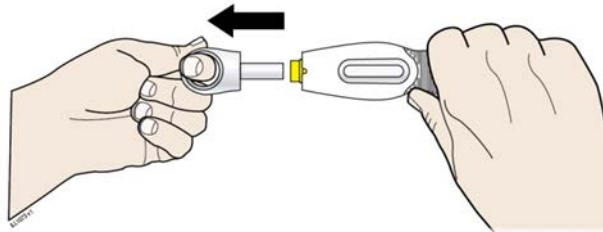
- The second injection should be given on a different site than the one used for the first injection. If you wish to use the same injection site, make sure it is not the exact same injection spot.
- Do not inject into areas where the skin is tender, bruised, red, hard, has scars, or stretch marks, or has raised thick, red, or scaly skin patches or lesions.
- Clean the area you are going to inject with an alcohol wipe. Let the skin dry before the injection.



- Do not touch this area again before injecting.

Step 2: Get ready

- D**
- Pull the white cap straight off just before the injection.
 - Once the cap is removed, the injection must be given within 5 minutes. There is no need to rush the injection - 5 minutes is enough time.

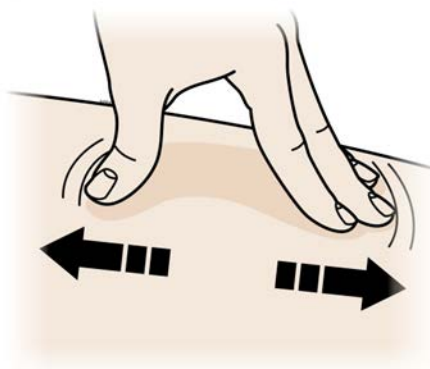


- Do not twist or bend the white cap.
- Discard the white cap in the special disposal container. Do not place the white cap back onto the pre-filled pen.
- Although hidden from view, the needle tip is now uncovered. Do not try to touch the needle as it could activate the pre-filled pen. It is normal to see a drop of liquid at the end of the needle (inside the yellow safety guard).

- E** Stretch or pinch the injection site to create a firm surface.

Stretch method

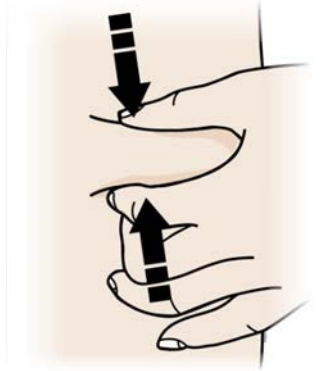
- Stretch the skin firmly by moving thumb and fingers in opposite directions, to create an area about 5 cm wide.



OR

Pinch method

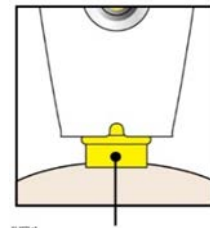
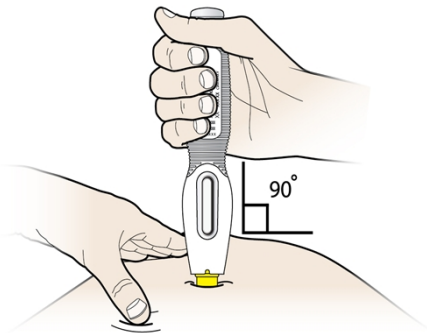
- Pinch the skin firmly between thumb and fingers, to create an area about 5 cm wide.



- **Important:** Keep the skin stretched or pinched while injecting.

Step 3: Inject

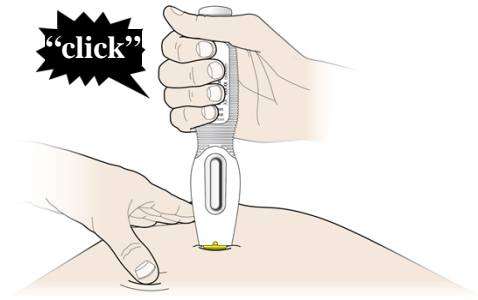
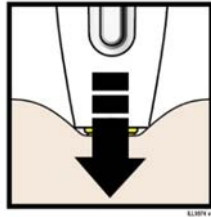
- F**
- **Important:** The pre-filled pen should not be pushed down until the actual injection is ready to be performed.
 - The stretch or pinch should be held. With the other hand, the pre-filled pen's yellow safety guard should be placed down on the area of the skin that previously has been cleaned (the "injection site") at a 90° degree angle.



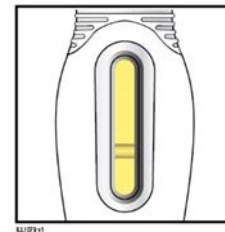
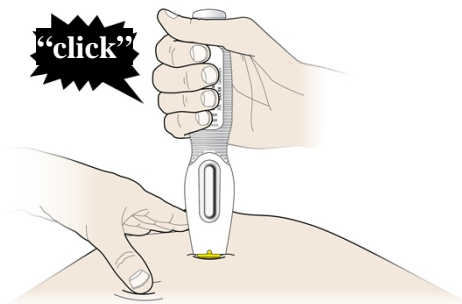
Yellow safety guard

- G**
- The pre-filled pen should be firmly pushed down onto the skin until the yellow safety guard stops moving. When you hear or feel a click, the injection will begin.
- H**
- **Keep pushing down on the skin.** The injection could take about 15 seconds.
 - When the injection is complete, the viewing window will turn fully yellow and you may also hear or feel a second click.

Push down



15 seconds

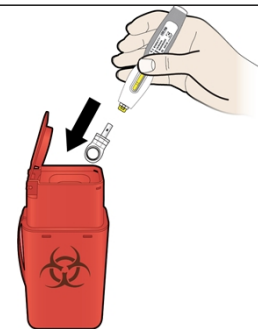


Window turns fully yellow when injection is complete.

- The used pre-filled pen may now be removed by carefully pulling it straight up from the skin.
- **Important:** When you remove the pre-filled pen, if the window has not turned fully yellow, or if it looks like the medicine is still injecting, this means the full dose has not been delivered. Your healthcare provider should be informed as soon as possible.
- After removing the pre-filled pen from the skin, the needle will be automatically covered. Do not try to touch the needle.

Step 4: Dispose

- I • Discard the entire used pre-filled pen and the white cap in a special container straight away after use.



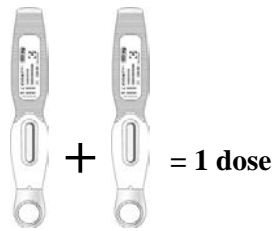
- Do not throw away (dispose of) the pre-filled pen in the household waste.
- Do not re-use the pre-filled pen.
- **Important:** Always keep the special disposal container out of the sight and reach of children.

Step 5: Examine the injection site

- J** If there is blood, use a cotton ball or a piece of gauze and apply light pressure over the injection site for a few seconds. Do not rub the injection site. The injection site can be covered with a small adhesive bandage, if necessary.

Step 6: Repeat for the second injection to get the full dose

- K** Repeat all steps starting from step C with the second pre-filled pen to inject the full dose. The second injection should be given on a different site than the one used for the first injection. If you wish to use the same injection site, make sure it is not the exact same injection spot.



Package leaflet: Information for the user

EVENTITY 105 mg solution for injection in a pre-filled syringe romosozumab

▼ This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.
- You will be given a patient alert card, which contains important safety information you need to be aware of before and during your treatment with EVENTITY.

What is in this leaflet

1. What EVENTITY is and what it is used for
2. What you need to know before you use EVENTITY
3. How to use EVENTITY
4. Possible side effects
5. How to store EVENTITY
6. Contents of the pack and other information

1. What EVENTITY is and what it is used for

What EVENTITY is

EVENTITY contains the active substance romosozumab, a medicine that helps to make the bones stronger, and reduce the risk of broken bones.

What EVENTITY is used for

EVENTITY is used to treat severe osteoporosis in women after the menopause who are at high risk of broken bone (fracture).

Osteoporosis is a disease that causes your bones to become thin and fragile. Many patients with osteoporosis have no symptoms, but they may be at increased risk of fractures.

How EVENTITY works

EVENTITY is a monoclonal antibody. A monoclonal antibody is a type of protein that has been designed to recognize and attach to specific proteins in the body. EVENTITY attaches to a protein called sclerostin. By attaching to and blocking the activity of sclerostin, EVENTITY:

- helps to form new bone, and
- slows down the loss of existing bone.

This makes the bones stronger, and lowers the risk of fractures.

2. What you need to know before you use EVENITY

Do not use EVENITY if:

- you are allergic to romosozumab or any of the other ingredients of this medicine (listed in section 6);
- you have low levels of calcium in the blood (hypocalcaemia). Your doctor will be able to tell you if your levels are too low;
- you have history of heart attack or stroke.

Do not use EVENITY if any of the above applies to you. If you are not sure, talk to your doctor or pharmacist before using EVENITY.

Warnings and precautions

Talk to your doctor or pharmacist and discuss your medical history before using EVENITY.

Heart attack and stroke

Heart attack and stroke have been reported in people receiving EVENITY.

Seek medical attention straight away if you get:

- chest pain, shortness of breath;
- headache, numbness, or weakness in your face, arms, or legs, difficulty talking, changes in vision, loss of balance.

Your doctor will carefully evaluate the risk of cardiovascular problems before he/she lets you start treatment with EVENITY. Tell your doctor if you know that you have an increased risk of cardiovascular problems such as established cardiovascular disease, high blood pressure, high blood fat levels, diabetes, smoking or kidney problems.

Low levels of calcium in the blood

EVENITY may cause low levels of calcium in your blood.

Tell your doctor if you notice:

- spasms, twitches, or cramps in your muscles;
- numbness or tingling in your fingers, toes or around your mouth.

Your doctor may prescribe calcium and vitamin D to help prevent low calcium levels in your blood before you start your treatment and while you take EVENITY. Take calcium and vitamin D as your doctor tells you to. Tell your doctor if you have or have ever had severe kidney problems, kidney failure or have needed dialysis as this may increase your risk of getting low blood calcium if you do not take calcium supplements.

Serious allergic reactions

Serious allergic reactions can happen to people who use EVENITY.

Seek medical attention straight away if you get:

- swelling of the face, mouth, throat, hands, feet, ankles, lower legs (angioedema), or hives;
- acute skin eruption showing multiple round, red/pink spots with a blistering or crusting centre (erythema multiforme);
- difficulty in swallowing or breathing.

Problems with your mouth, teeth or jaw

A side effect called osteonecrosis of the jaw (ONJ) (bone damage in the jaw) has been reported rarely (may affect up to 1 in 1,000 people) in patients receiving EVENITY. ONJ can also occur after stopping treatment. It is important to try to prevent ONJ developing as it may be a painful condition that can be difficult to treat. In order to reduce the risk of developing ONJ, there are some precautions you should take.

Before receiving EVENITY, tell your doctor or nurse if you:

- have any problems with your mouth or teeth such as poor dental health, gum disease, or a planned tooth extraction;
- do not receive routine dental care or have not had a dental check-up for a long time;
- are a smoker (as this may increase the risk of dental problems);
- have previously been treated with a bisphosphonate (used to treat or prevent bone disorders, such as osteoporosis);
- are taking medicines called corticosteroids (such as prednisolone or dexamethasone);
- have cancer.

Your doctor may ask you to undergo a dental examination before you start treatment with EVENITY.

While being treated, you should maintain good oral hygiene and receive routine dental check-ups. If you wear dentures, you should make sure these fit properly. If you are under dental treatment or will undergo dental surgery (e.g. tooth extractions), inform your doctor about your dental treatment and tell your dentist that you are being treated with EVENITY.

Contact your doctor and dentist immediately if you get any problems with your mouth or teeth such as:

- loose teeth;
- pain or swelling;
- mouth sores that do not heal;
- discharge.

Unusual thigh bone fractures

People who have used EVENITY, rarely developed unusual fractures of the thigh bone caused by little or no trauma. These fracture types are often preceded by warning signs of thigh or groin pain for several weeks before the fracture occurs. It is not known whether EVENITY caused these unusual fractures. Tell your doctor or pharmacist if you get any new or unusual pains in your hip, groin or thigh.

Children and adolescents

The use of romosozumab in children and adolescents has not been studied and it is not approved for use in paediatric patients (age <18 years).

Other medicines and EVENITY

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Pregnancy and breast-feeding

EVENITY is only intended to treat women after menopause.

EVENITY should not be used by women of child-bearing potential, or when pregnant or breast-feeding. It is not known whether EVENITY may harm an unborn or breast-fed child.

Contact your doctor if you have any questions.

Driving and using machines

EVENITY is expected to have no effect or very little effect on the ability to drive and use machines.

EVENITY contains sodium

This medicine contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'.

3. How to use EVENITY

EVENITY will be initiated and supervised by specialist physicians experienced in the management of osteoporosis. Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure.

The injection should only be given by a person who has been properly trained.

How much to use

- The recommended dose of EVENITY is 210 mg.
- Since one pre-filled syringe contains 105 mg of the active substance romosozumab, 2 pre-filled syringes must be used for each dose. The second injection must be given immediately after the first one but at a different injection site.
- Do this once every month for 12 months.

How to use

- EVENITY has to be injected under the skin (sub-cutaneous injection).
- EVENITY should be injected in either the stomach area (abdomen) or thigh. The outer area of your upper arm can also be used as an injection site, but only if someone else is giving you the injection.
- If the same injection area is planned to be used for the second injection, a different injection spot should be used.
- EVENITY should not be injected into areas where the skin is tender, bruised, red, or hard.

It is important that you read the **Instructions for Use** for detailed information on how to use the EVENITY pre-filled syringe.

Ask your doctor or pharmacist if you have any further questions on the use of the medicine.

If you use more EVENITY than you should

If, by mistake, you have used more EVENITY than you should, contact your doctor or pharmacist.

If you forget to use or cannot take EVENITY at your usual time

If you miss a dose of EVENITY, contact your doctor as soon as possible to schedule another dose. Thereafter, the next dose should be given not earlier than one month after the date of the last dose.

If you stop taking EVENITY

If you are considering stopping EVENITY treatment, please discuss this with your doctor. Your doctor will advise you on how long you should be treated with EVENITY.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

Discuss with your doctor the need to switch to another osteoporosis treatment after the end of your treatment with EVENITY.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Seek medical attention straight away if you get the following possible symptoms of **heart attack** or **stroke** (uncommon: may affect up to 1 in 100 people):

- chest pain, shortness of breath;
- headache, numbness, or weakness in your face, arms, or legs, difficulty talking, changes in vision, loss of balance.

Seek medical attention straight away if you get the following symptoms of **serious allergic reaction** (rare: may affect up to 1 in 1,000 people):

- swelling of the face, mouth, throat, hands, feet, ankles, lower legs (angioedema), or hives;
- acute skin eruption showing multiple round, red/pink spots with a blistering or crusting centre (erythema multiforme);
- difficulty in swallowing or breathing.

Tell your doctor if you notice the following symptoms of **low levels of calcium** in the blood (hypocalcaemia) (uncommon: may affect up to 1 in 100 people):

- spasms, twitches, or cramps in your muscles;
- numbness or tingling in your fingers, toes or around your mouth.

See also section 2 “What you need to know before you use EVENITY”.

Other side effects may include:

Very common side effects (may affect more than 1 in 10 people):

- Common cold;
- Joint pain.

Common side effects (may affect up to 1 in 10 people):

- Rash, inflammation of the skin;
- Headache;
- Sinusitis;
- Neck pain;
- Muscle spasms;
- Redness or pain around the site where the injection was given.

Uncommon side effects (may affect up to 1 in 100 people):

- Hives (urticaria);
- Cataract.

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via [the national reporting system listed in Appendix V](#). By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store EVENITY

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label and carton after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C - 8°C). Do not freeze.

Once you take the carton containing the pre-filled syringes out of the refrigerator for use, you should not put it back into the refrigerator but you can keep it at room temperature (up to 25°C) for up to 30 days. If not used within this period the product should be discarded.

Keep the pre-filled syringe in the outer carton in order to protect from light.

Visually check the solution. Do not use it if the solution is discoloured, cloudy, or contains flakes or particles.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What EVENITY contains

- The active substance is romosozumab. Each pre-filled syringe contains 105 mg of romosozumab in 1.17 ml of solution (90 mg/ml).
- The other ingredients are calcium acetate, glacial acetic acid, sodium hydroxide (for pH adjustment), sucrose, polysorbate 20 and water for injections. See section 2 “EVENITY contains sodium.”

What EVENITY looks like and contents of the pack

EVENITY is a clear to opalescent, colourless to light yellow solution for injection provided in a single use disposable pre-filled syringe. The syringe is made of plastic with a stainless steel needle.

Pack size of 2 pre-filled syringes.

Multipack containing 6 (3 packs of 2) pre-filled syringes.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

UCB Pharma S.A., Allée de la Recherche 60, B-1070 Bruxelles, Belgium

Manufacturer:

Amgen Europe B.V., Minervum 7061, 4817 ZK Breda, Netherlands

For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder.

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This leaflet was last revised in MM/YYYY.

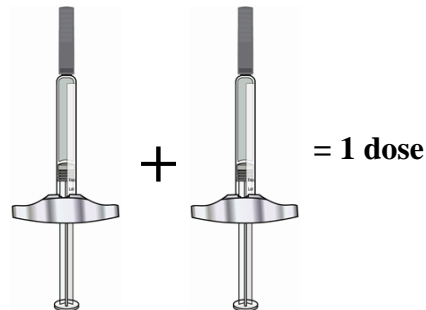
Other sources of information

Detailed information on this medicine is available on the European Medicines Agency web site:
<http://www.ema.europa.eu>.

Please turn over for the Instructions for Use.

INSTRUCTIONS FOR USE FOR THE EVENTY INJECTION BY MEANS OF A PRE-FILLED SYRINGE

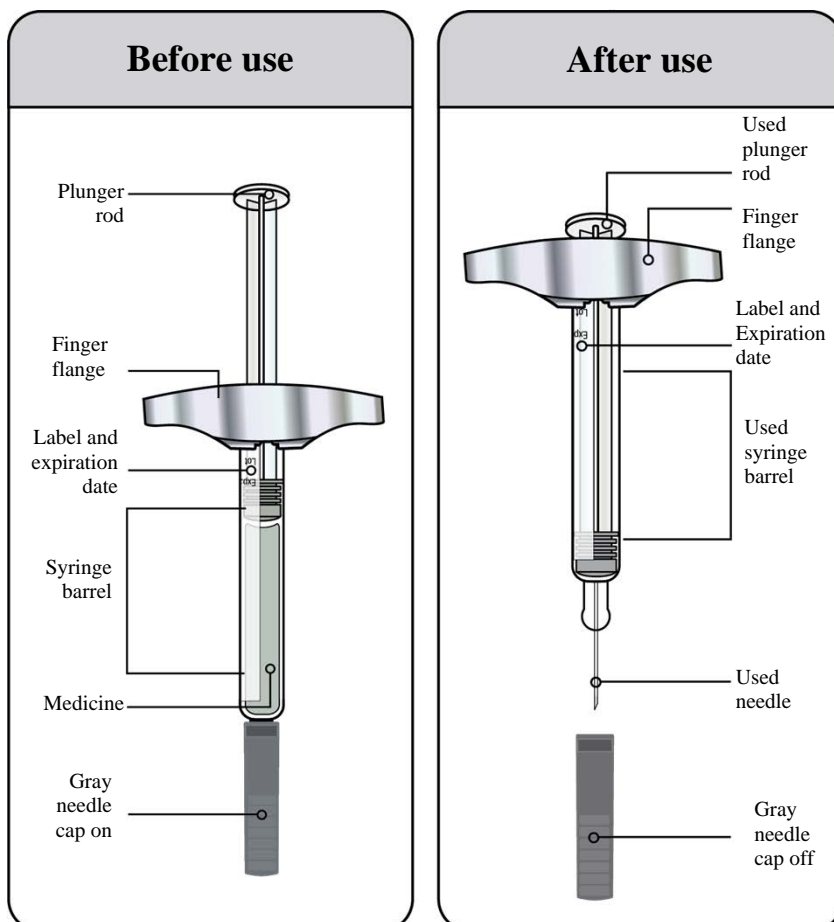
Inject two pre-filled syringes one immediately after the other to get a full dose



The following instructions explain how to use the pre-filled syringe to inject EVENTY.

- **Please read these instructions carefully and follow them step by step.**
- If you have any questions or you feel unsure about the injection procedure, please contact a doctor or pharmacist.
- It is important to make sure that the injection is only administered by an individual that has been properly trained.
- The pre-filled syringe is also referred to as “the medicine”.

Guide to parts: pre-filled syringe

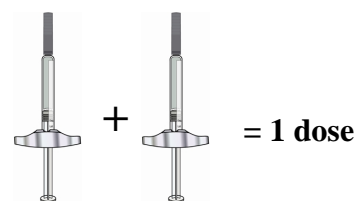


STOP



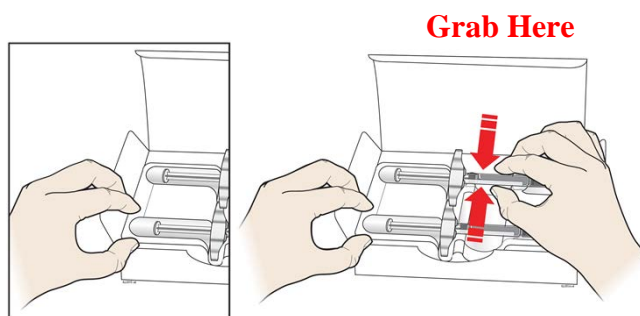
Read this before the medicine is injected.

Your healthcare provider has prescribed a dose of 210 mg every month dose: **To receive your full dose, two 105 mg pre-filled syringes should be injected, one immediately after the other.**



Step 1: Prepare

- A
- Take the carton containing the two pre-filled syringes out of the refrigerator.
 - Your pre-filled syringes should be left outside the refrigerator to reach room temperature (up to 25°C) **for at least 30 minutes** before injection (do not warm in any other way). This will make the injection more comfortable.
 - Open the carton and gather all the materials you need for the injection (as listed in Step B).
 - Wash your hands thoroughly.
 - Remove **two** pre-filled syringes from the carton as shown in the picture.
 - **Important:** Always hold the pre-filled syringes by the syringe barrel.
 - Place finger or thumb on edge of tray to secure it while you remove the pre-filled syringes.
 - Grab the syringe barrel to remove the pre-filled syringes from the tray.



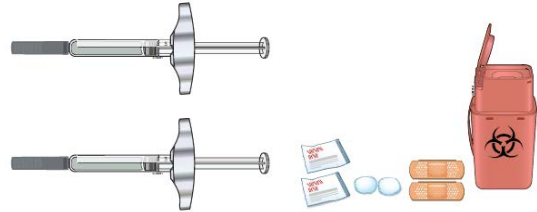
- Do not grasp the plunger rod or the grey needle cap.
- Do not remove the grey cap from the pre-filled syringes yet.
- Do not remove the finger flange. This is part of the pre-filled syringe.
- Do not shake the pre-filled syringes.
- Check the medicine in the syringes. The medicine should be a clear to opalescent, colourless to light yellow solution.
 - Do not use the pre-filled syringes if the solution is discoloured, cloudy, or contains flakes or particles.
 - You may see air bubbles. Injecting the solution subcutaneously (under the skin) which contains air bubbles is harmless.

- Do not use the pre-filled syringe if:
 - it has been dropped;
 - if the grey needle cap is missing or not securely attached;
 - if the seal is missing or broken or if any part appears cracked or broken.

In such case, use a new syringe and contact your doctor as soon as possible.

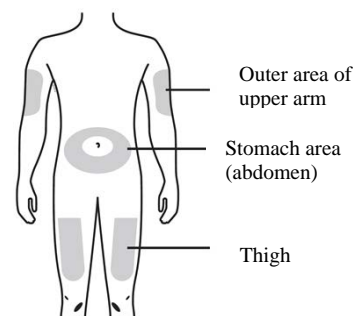
B On a clean, well-lit work surface, place:

- **two** pre-filled syringes;
- two alcohol wipes;
- two cotton balls or gauze pads;
- two adhesives bandages;
- special disposal container.

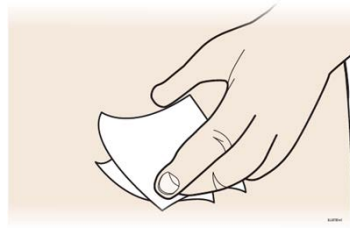


C Prepare and clean the skin where you are going to inject the medicine. You can choose from:

- the thighs;
- the stomach area (abdomen), but not the 5 cm area around the belly button;
- the outer area of the upper arm (if someone else is giving you the injection).



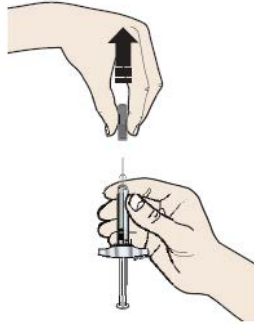
- The second injection should be given on a different site than the one used for the first injection. If you wish to use the same injection site, make sure it is not the exact same injection spot.
- Do not inject into areas where the skin is tender, bruised, red, hard, has scars, or stretch marks, or has raised thick, red, or scaly skin patches or lesions
- Clean the area you are going to inject with an alcohol wipe. Let the skin dry before the injection.



- Do not touch this area again before injecting.

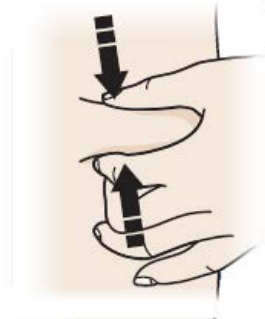
Step 2: Get ready

- D**
- Pull the grey needle cap straight off and away from the body just before the injection.
 - Take care not to touch the needle or let the needle touch any surface.
 - Once the cap is removed, the injection must be given within 5 minutes. There is no need to rush the injection - 5 minutes is enough time.
 - It is normal to see a drop of liquid at the end of the needle.



- Do not twist or bend the grey needle cap.
- Discard the grey needle cap in the special disposal container. Do not place the grey needle cap back onto the pre-filled syringe.

- E** • Pinch skin firmly between your thumb and fingers, creating a firm surface about 5 cm wide.



- **Important:** Keep the skin pinched while injecting.

Step 3: Inject

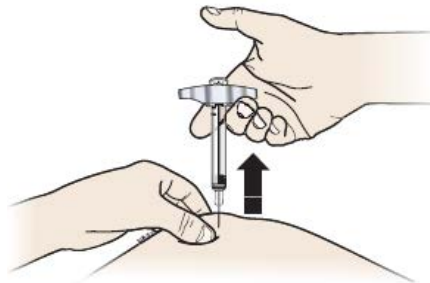
- F** • **Important:** The plunger rod should not be pushed down until the actual injection is ready to be performed.
- The pinch should be held. With the other hand, the pre-filled syringe's needle should be inserted into the area of the skin that previously has been cleaned (the "injection site") at a 45 to 90° degree angle.
 - Finger should not be placed on the plunger rod while inserting the needle.



- G** • Using slow and constant pressure, push the plunger rod all the way down until it stops moving indicating the entire dose has been delivered. The pre-filled syringe should be kept in the skin while completing the dose delivery.



- H** • Once complete, release your thumb and gently lift the pre-filled syringe off the skin at the same angle at which it was inserted.
- After you remove the pre-filled syringe from the skin, the syringe barrel should be empty.



- **Important:** If it looks like the medicine is still in the syringe barrel, this means you have not delivered a full injection. Your healthcare provider should be informed as soon as possible.

Step 4: Dispose

- I** • Discard the entire used pre-filled syringe and the grey needle cap in a special container straight away after use.



- Do not throw away (dispose of) the pre-filled syringe in the household waste.
- Do not re-use the pre-filled syringe.
- **Important:** Always keep the special disposal container out of the sight and reach of children.

Step 5: Examine the injection site

- J** If there is blood, use a cotton ball or piece of gauze and apply light pressure over the injection site for a few seconds. Do not rub the injection site. The injection site can be covered with a small adhesive bandage, if necessary.

Step 6: Repeat for the second injection to get the full dose

- K** Repeat all steps starting from step C with the second pre-filled syringe to inject the full dose. The second injection should be given on a different site than the one used for the first injection. If you wish to use the same injection site, make sure it is not the exact same injection spot.

