Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) – 1986

The medicine is dispensed according to a doctor's prescription only

EVENITY 105 mg, solution for subcutaneous injection

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

List of the additional ingredients detailed in section 6.

Read the entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have any other questions, refer to the doctor or the pharmacist.

This medicine has been prescribed for you. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

In addition to the patient leaflet, **Evenity** has patient safety information card. This card includes important safety information that you should know, before treatment initiation and during the treatment with **Evenity** and act according to it. The patient safety information card and the patient leaflet should be read prior treatment initiation with this product. The card should be kept for additional reading as needed.

WARNING: potential risk of a heart attack, stroke and death as a result of a cardiovascular problem

- **Evenity may increase the risk of a heart attack, stroke, and death as a result of a cardiovascular problem. Evenity treatment should not be initiated in patients who have had a heart attack or stroke within the preceding year. The doctor will consider whether the benefits outweigh the risks in patients with other cardiovascular problems. If a patient experiences a heart attack or stroke during therapy, evenity should be discontinued.**

1. What is the medicine intended for?

Evenity is indicated to treat severe osteoporosis (bone thinning) in women after the menopause who are at high risk of broken bone (fracture), defined as a history of osteoporotic bone fracture, or having a number of risk factors for fracture; or when other osteoporosis treatment did not work well or when the patient cannot use another osteoporosis medicine.

Evenity is not intended to be used by children and adolescent under 18 years old.

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.

Therapeutic group:
Medicinal products for treatment of bone diseases, medicinal products affecting bone structure and mineralization**.**

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

Evenity 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. **Evenity** attaches to a protein called sclerostin. By attaching to and blocking the activity of sclerostin, **Evenity**:

- 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. Before using the medicine

Do not use the medicine if:
- you are sensitive (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 within the preceding year.

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**.

Special warnings regarding the use of the medicine
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 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.

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.

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.

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 (and receives treatments such as chemotherapy and inhibitors of new blood vessels' growth (angiogenesis inhibitors));
- are taking medicines containing denosumab.

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 proceded 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

There are no safety and efficacy data for the use of **Evenity** in children and adolescents.

Other medicines and Evenity

If you are taking, or have recently taken, other medicines including non-prescription medicines and food supplements, tell the doctor or the pharmacist.

Pregnancy, breast-feeding and fertility

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.

Important information about some ingredients of the medicine

Evenity contains sodium

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

3. How should you use the medicine?

EVENITY will be initiated and supervised by specialist physicians experienced in the management of osteoporosis.
Always use according to the doctor's instructions.

The first dose of EVENITY should be administered by a healthcare provider only. Starting from the second dose, the injection can be performed by an individual who has been properly trained by a healthcare provider only.

You should check with the doctor or the pharmacist if you are unsure.
The dosage and treatment will be determined only by the doctor.

- The usual 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.
- **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.

Do not exceed the recommended dose.
If you have taken an overdose or if a child has accidentally swallowed the medicine, refer immediately to a doctor or to a hospital emergency room and bring the package of the medicine with you.

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.

Persist with the treatment as recommended by the doctor.

If you stop taking the medicine
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**.

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

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.

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

4. Possible side effects

As with any medicine, use of **Evenity** may cause side effects in some of the users. Do not be alarmed by reading the list of side effects. You may not experience any of 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 "Before using the medicine".

Other side effects may include:

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

- Joint pain.

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

- Rash;
- Headache;
- 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):

- Inflammation of the skin;
- Hives (urticaria).

If a side effect has appeared, if any of the side effects get worse or when you suffer from a side effect that has not been mentioned in the leaflet, you should consult the doctor.

Reporting of side effects
Side effects can be reported to the Ministry of Health by clicking on the link "reporting of side effects due to medical treatment" found on the Ministry of Health homepage (**www.health.gov.il)** which directs you to the online form for reporting side effects, or by entering the link: **https://sideeffects.health.gov.il**

5. How to store the medicine

Avoid poisoning! This medicine and any other medicine should be kept in a closed place out of the sight and reach of children and/or infants to avoid poisoning. Do not induce vomiting without an explicit instruction from the doctor.

Do not use the medicine after the expiry date (exp. date) appearing on the package. The expiry date refers to the last day of that month.

Store in a refrigerator (2°C - 8°C). Do not freeze. Do not shake.
Keep the pre-filled syringe in the original carton in order to protect from light.
If removed from the refrigerator, **Evenity** can be kept at room temperature up to 25°C in the original carton and must be used within 30 days. If not used within 30 days, discard **Evenity**.

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. Additional information

In addition to the active ingredient the medicine also contains: acetate, calcium, polysorbate 20 and sucrose in Water for Injection, USP, and sodium hydroxide to a pH of 5.2.

What does the medicine look like and what is the content of the package:
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.

Manufacturer:
Amgen Inc.
Thousand Oaks, California 91320-1799
USA

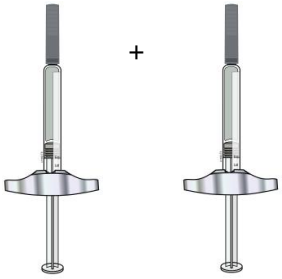
License Holder:
Amgen Europe B.V., P.O. BOX 53313, Tel - Aviv.

Approved in June 2020.

Registration number of the medicine in the National Drug Registry of the Ministry of Health:
164-77-36165

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

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

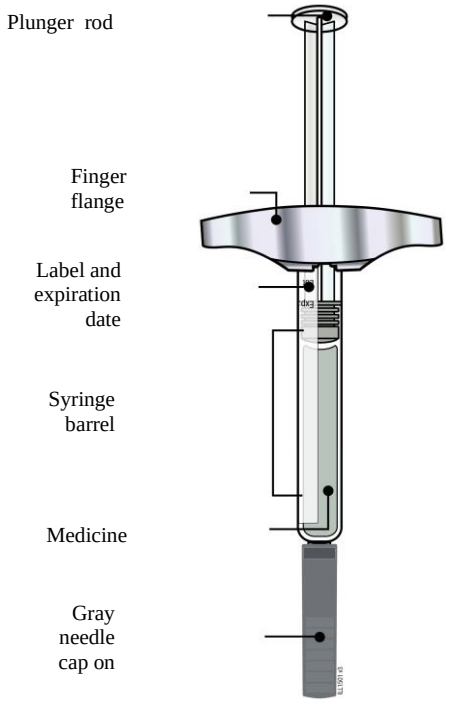
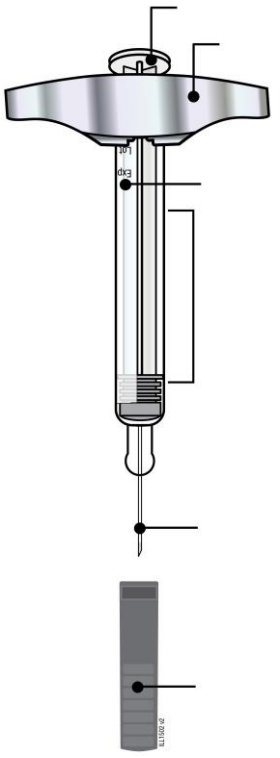


= 1 dose

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

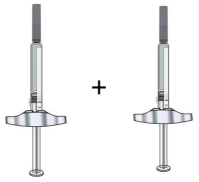
- **Please read these instructions carefully and follow them step by step.**
- If you have any questions or you feel unsure about the injection procedure, please contact a doctor or pharmacist.
- The first dose of EVENITY should be administered by a healthcare provider only. Starting from the second dose, the injection can be performed by an individual who has been properly trained by a healthcare provider only.
- The pre-filled syringe is also referred to as “the medicine”.

Guide to parts: pre-filled syringe

Before use	After use
	

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, <u>two 105 mg pre-filled syringes should be injected,</u> one immediately after the other**.



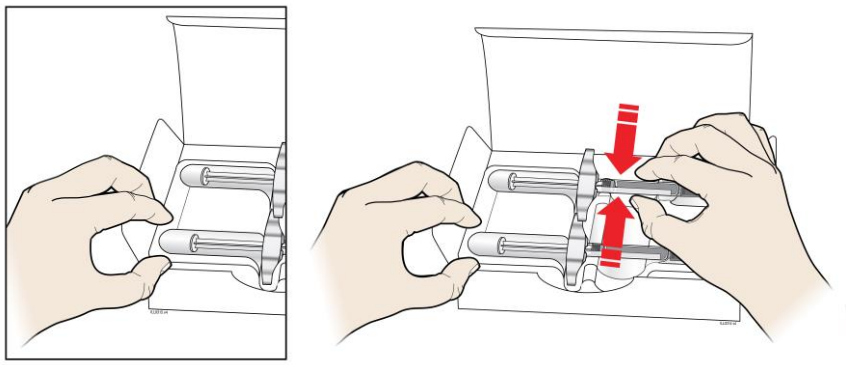
= 1 dose

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.

Grab Here

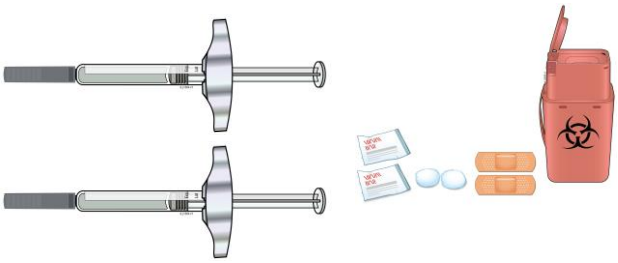


- Do not grasp the plunger rod or the grey needle cap.
- Do not remove the grey cap from the pre-filled syringes yet.
- Do not remove the finger flange. This is part of the pre-filled syringe.
- Do not shake the pre-filled syringes.
- Check the medicine in the syringes. The medicine should be a clear 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.

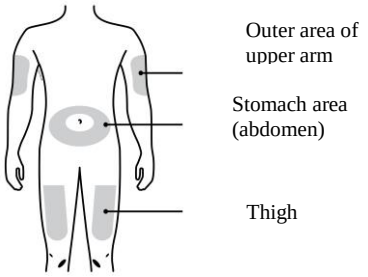
B On a clean, well-lit work surface, place:

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

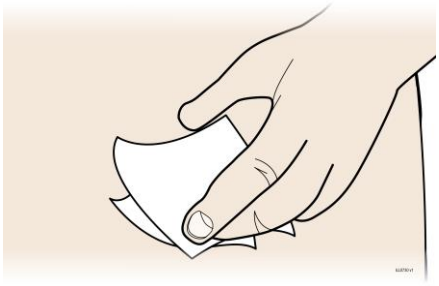


C Prepare and clean the skin where you are going to inject the medicine. You can choose from:

- 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.

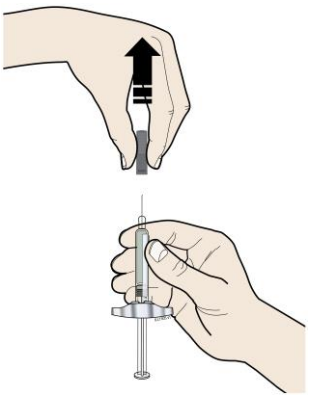


- Do not touch this area again before injecting.

Step 2: Get ready

D

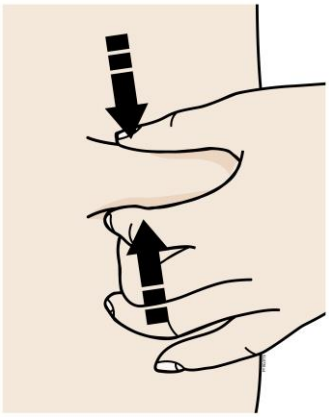
- Pull the grey needle cap straight off and away from the body just before the injection.
  - Take care not to touch the needle or let the needle touch any surface.
- Once the cap is removed, the injection must be given within 5 minutes. There is no need to rush the injection - 5 minutes is enough time.
  - 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.

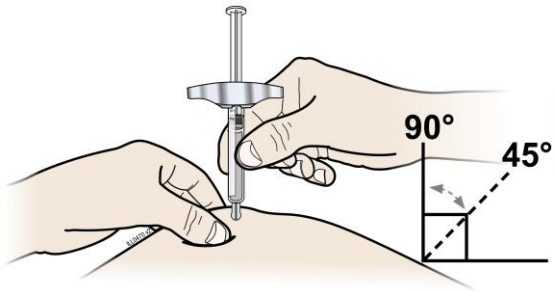


- **Important:** Keep the skin pinched while injecting.

Step 3: Inject

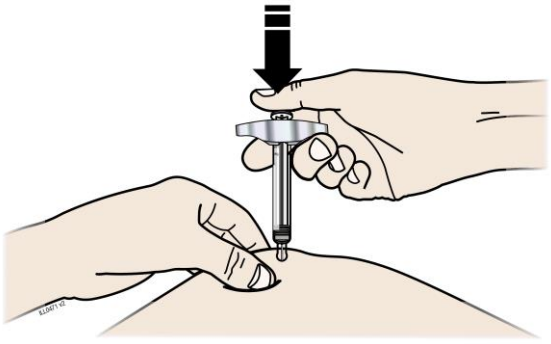
F

- **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.



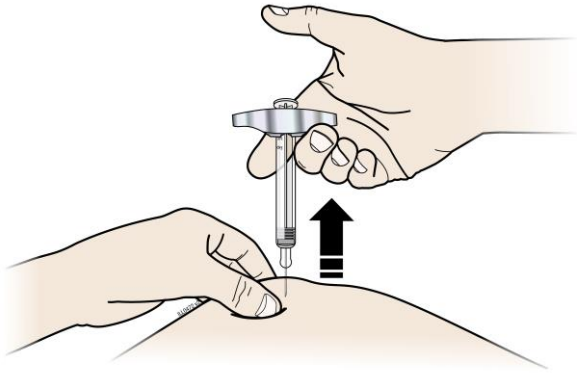
G

- 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.

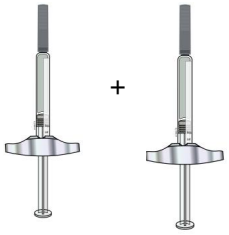
- Do not throw away (dispose of) the pre-filled syringe in the household waste.
- Do not re-use the pre-filled syringe.
- **Important:** Always keep the special disposal container out of the sight and reach of children.

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.



+

= 1 dose