

Patient leaflet in accordance with the Pharmacists' Regulation (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only.

Repatha

140 mg solution for injection in pre-filled syringe

140 mg solution for injection in pre-filled pen

Active Ingredient

The active substance is evolocumab.

- Each pre-filled syringe contains 140 mg of evolocumab in 1 mL of solution.
- Each pre-filled pen contains 140 mg of evolocumab in 1 mL of solution.

For Inactive ingredients and allergens in the medicine – see section 6 “Additional information”
Read this leaflet carefully and until the end before using this medicine. This leaflet contains essential information about the medicine. If you have additional questions, contact your doctor or pharmacist.

This medicine is prescribed for treating your illness. Do not pass it on to others. It may cause them harm even if it appears to you that their illness is similar.

1. What is this Medicine Intended for?

Hypercholesterolemia and mixed dyslipidemia

Repatha is indicated in adults with primary hypercholesterolemia (heterozygous familial and non-familial; condition of high cholesterol level in the blood) or mixed dyslipidemia (disorder in various lipids level in the blood). The medicine is given as an adjunct to diet:

- in combination with a statin or statin with other lipid-lowering therapies in patients unable to reach the goals set for cholesterol levels with the maximum tolerated dose of a statin.
- alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.

Homozygous familial hypercholesterolemia (condition of high cholesterol level in the blood)

Repatha is indicated in adults and adolescents aged 12 years and over with homozygous familial hypercholesterolemia in combination with other lipid-lowering therapies.

Established atherosclerotic cardiovascular disease

Repatha is indicated in adults with established atherosclerotic cardiovascular disease (a history of myocardial infarction, stroke or peripheral arterial disease) to reduce cardiovascular risk by lowering cholesterol levels. The medicine is given as an adjunct to reduce other risk factors:

- in combination with the maximum tolerated dose of a statin with or without other lipid-lowering therapies.
- alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated.

Therapeutic group: Repatha is a human monoclonal antibody that helps lowering blood cholesterol levels.

Repatha is a medicine that lowers levels of 'bad' cholesterol (LDL), a type of fat, in the blood.

Repatha contains the active substance evolocumab, a monoclonal antibody (a type of specialized protein designed to attach to a target substance in the body). Evolocumab is designed to attach to a substance called PCSK9 that affects the liver's ability to take in cholesterol. By attaching to, and mopping up PCSK9, the medicine increases the amount of cholesterol entering the liver and so lowers the level of cholesterol in the blood.

Repatha is used in patients who cannot control their cholesterol levels with a cholesterol lowering diet alone. You should stay on your cholesterol lowering diet while taking this medicine. Repatha can help prevent heart attack, stroke, and certain heart procedures to restore blood flow to the heart due to a build-up of fatty deposits in your arteries (also known as atherosclerotic cardiovascular disease).

2. Before Using this Medicine

X Don't use this medicine if:

- you are sensitive (allergic) to the active ingredient evolocumab or to any of the additional ingredients in this medicine (refer to list of inactive ingredients in section 6 – “Additional Information”)

! Special warnings regarding the usage of the medicine

Talk to your doctor, pharmacist or nurse before using Repatha if you have:

- liver disease,
- severe kidney problems.

The needle cover of the glass pre-filled syringe and pen is made from dry natural rubber (a derivative of latex), which may cause allergic reactions.

! Children and adolescents

The use of Repatha has not been studied in children under 18 years of age being treated for primary hypercholesterolemia and mixed dyslipidemia.

The use of Repatha has not been studied in children under 12 years of age being treated for homozygous familial hypercholesterolemia.

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

! Taking this medicine and food

There is no known interaction with food.

! Taking this medicine and alcohol consumption

There is no known interaction with alcohol.

! Pregnancy and breast-feeding

If you are pregnant, think you may be pregnant or trying to get pregnant consult with your doctor or pharmacist before use.

Repatha has not been tested in pregnant women. It is not known if Repatha will harm your unborn baby.

It is not known whether Repatha is found in breast milk.

It is important to tell your doctor if you are breast-feeding or plan to do so. Your doctor will then help you decide whether to stop breast-feeding, or whether to stop taking Repatha, considering the benefit of breast-feeding to the baby and the benefit of Repatha to the mother.

! Driving and using machines

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

! Important information on part of the medicine ingredients

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

3. How to use this Medicine?

Always use this medicine exactly as your doctor has told you. Check with your doctor or a pharmacist if you are not sure.

The dosage and treatment will be determined by the doctor only. The recommended dosage usually is

- for adults with primary hypercholesterolemia and mixed dyslipidemia the dose is either 140 mg every two weeks or 420 mg once monthly.
- for adults or adolescents with homozygous familial hypercholesterolemia the recommended starting dose is 420 mg once monthly. After 12 weeks your doctor may decide to increase the dose to 420 mg every two weeks. If you also receive apheresis, a procedure similar to dialysis where cholesterol and other fats are removed from the blood, your doctor may decide to start you on a dose of 420 mg every two weeks to coincide with your apheresis treatment.
- for adults with established atherosclerotic cardiovascular disease (a history of heart attack, stroke or blood vessel problems) the dose is either 140 mg every two weeks or 420 mg once monthly.

If your doctor prescribes a dose of 420 mg you must use three pre-filled syringes or pre-filled pens because each pre-filled syringe or pre-filled pen only contains 140 mg of medicine. After reaching room temperature, all injections should be given within a 30 minute period.

Repatha is given as an injection under the skin: subcutaneous (SC).

If your doctor decides that you or a caregiver can give the injections of Repatha, you or your caregiver should receive training on how to prepare and inject Repatha correctly. Do not try to inject Repatha until you have been shown how to do it by your doctor or nurse.

See the detailed “Instructions for Use” at the end of this leaflet for instructions about how to store, prepare, and give your Repatha injections at home. If using the pre-filled pen, **place the correct (yellow) end of the pen on the skin before injecting.**

Before starting Repatha, you should be on a diet to lower your cholesterol. You should keep on this cholesterol lowering diet while taking Repatha.

If your doctor has prescribed Repatha along with another cholesterol lowering medicine, follow your doctor’s instructions on how to take these medicines together. In this case, please read the dosage instructions in the package leaflet of that particular medicine as well.

If you accidentally took a higher dose

Contact your doctor or pharmacist immediately.

If you forgot to take the medicine

Take Repatha as soon as you can after the missed dose. Then, contact your doctor who will tell you when you should schedule your next dose, and follow the new schedule exactly as your doctor has told you.

If you stop treatment with the medicine

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting first with the doctor.

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

If you have any additional questions regarding the usage of this medicine, consult a doctor or a pharmacist.

4. Side Effects

Like any medicine, using Repatha may cause side effects in some of the users. Do not be alarmed by reading the list of side effects. It is possible that you will not suffer from any one of them.

Stop the medicine and refer to the doctor immediately if you develop an allergic reaction to the medicine.

Common side effects: may affect 1 - 10 out of 100 treated patients:

- Flu (high temperature, sore throat, runny nose, cough and chills)
- Common cold, such as runny nose, sore throat or sinus infections (nasopharyngitis or upper respiratory tract infections)
- Feeling sick (nausea)
- Back pain
- Joint pain (arthralgia)
- Muscle pain
- Injection site reactions, such as bruising, redness, bleeding, pain or swelling
- Allergic reactions including rash
- Headache

Uncommon side effects: may affect 1 - 10 out of 1000 treated patients:

- Hives, red itchy bumps on your skin (urticaria)
- Flu-like symptoms

Rare side effects: may affect 1 - 10 out of 10,000 treated patients:

- Swelling of the face, mouth, tongue, or throat (angioedema)

Reporting of side effects

You can report adverse reactions to the Ministry of Health by clicking on the link "report on adverse reactions following medication treatment" located on the homepage of the Ministry of Health website (www.health.gov.il) referring to the online form for reporting adverse reactions or by using the link: <https://sideeffects.health.gov.il/>

5. How to Store the Medicine?

- Avoid toxicity! This medicine and any other medicine should be stored in a closed place, out of the sight and reach of children, thereby preventing toxicity. Do not cause vomiting without an explicit instruction from a doctor.
- Don't use this medicine after the expiry date (EXP) that appears on the package and blister. The expiry date refers to the last day of that particular month.
- Store in a refrigerator at 2°C to 8°C.
- Store in the original package to protect from light.
- When removed from the refrigerator, Repatha should be kept at room temperature (up to 25°C) in the original carton up to 30 days.
- Do not freeze.
- Do not shake.
- Do not throw away the medicine via wastewater or household waste. Ask your doctor or pharmacist how to throw away medicines.
- Do not use if any part of the pre-filled syringe or pen appears cracked or broken.
- Do not use if the grey needle cap on the pre-filled syringe is missing or not securely attached.
- Do not use if the medicine is discolored or contains large lumps, flakes or particles.

6. Additional Information

In addition to the active ingredient, this medicine also contains:

- Proline,
- Glacial acetic acid,
- Polysorbate 80,
- Sodium hydroxide,
- Water for injections.

How the medicine looks and what is the content of the package?

Repatha is a solution which is clear to opalescent, colorless to yellowish, and practically free from particles.

Do not use this medicine if you notice it is discolored or contains large lumps, flakes or colored particles.

Each pack contains one single-use pre-filled syringe.

Each pack contains one, two, three or six single-use SureClick pre-filled pens.

Not all pack sizes may be marketed.

Registration Holder's name and address:

Amgen Europe B.V.

P.O. BOX 53313, Tel - Aviv, Israel.

Manufacturer's name and address:

Amgen Europe B.V.

Minervum 7061, Breda, The Netherlands.

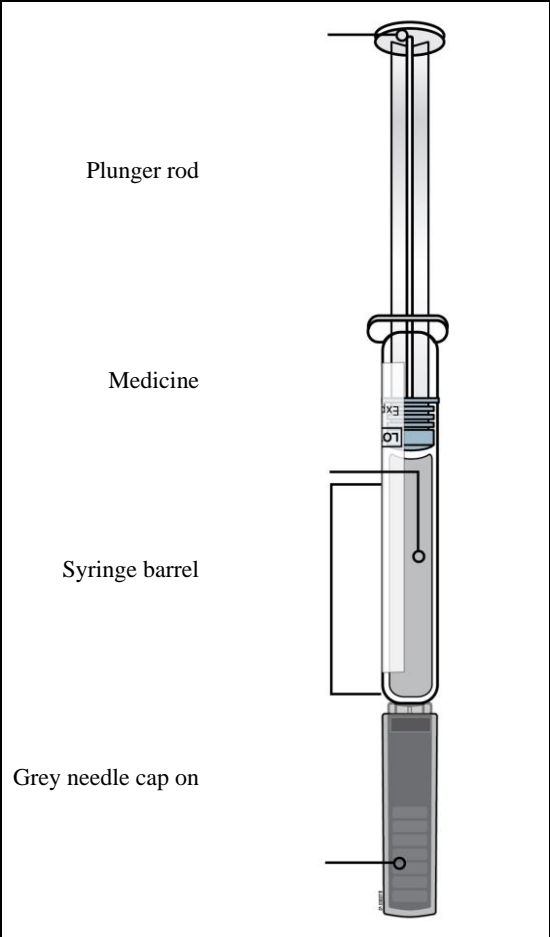
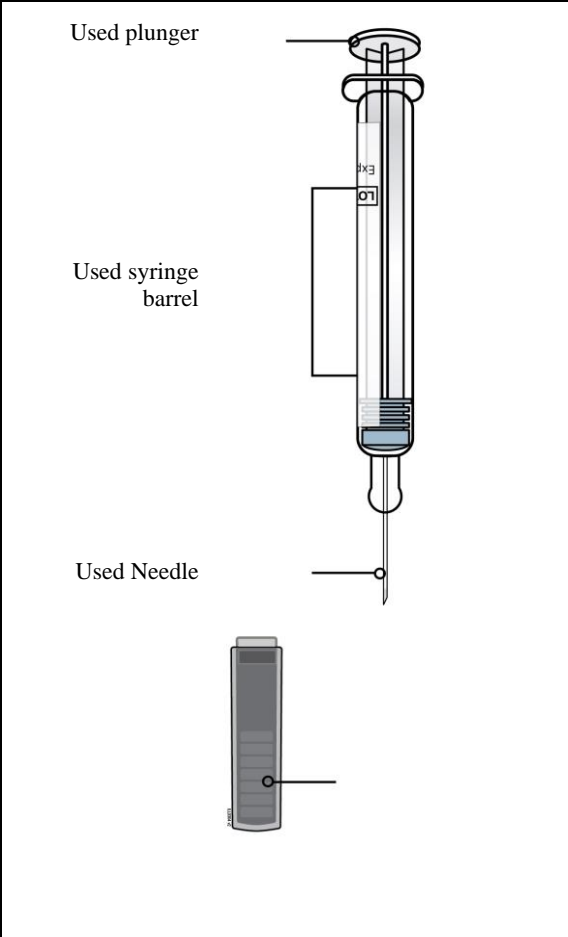

Revised in May 2021 according to MoHs guidelines.

Registration number of the medicine in the National Drugs Registry at the Ministry of Health:

155 71 34521

Instructions for use:
Repatha single-use pre-filled syringe

Guide to parts

Before use	After use
	
	Needle is inside.

Important

Before you use a Single-Use Repatha Pre-filled Syringe, Read this Important Information:

- **Do not** freeze or use the Repatha pre-filled syringe if it has been frozen.
- **Do not** use the Repatha pre-filled syringe if the packaging is open or damaged.
- **Do not** use the Repatha pre-filled syringe if it has been dropped onto a hard surface. Part of the syringe may be broken even if you cannot see the break. Use a new Repatha pre-filled syringe.
- **Do not** remove the grey needle cap from the Repatha pre-filled syringe until you are ready to inject.

Step 1: Prepare

A Remove the Repatha pre-filled syringe carton from the refrigerator and wait 30 minutes.

Wait at least 30 minutes for the pre-filled syringe in the carton to naturally reach room temperature before injecting.

Check that the name Repatha appears on the carton label.

- **Do not** try to warm the Repatha pre-filled syringe by using a heat source such as hot water or microwave.
- **Do not** leave the Repatha pre-filled syringe exposed to direct sunlight.
- **Do not** shake the Repatha pre-filled syringe.

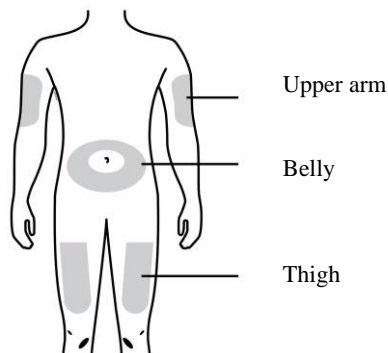
B Gather all materials needed for your injection.

Wash your hands thoroughly with soap and water.

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

- One Repatha pre-filled syringe in its tray.
- Alcohol wipes.
- Cotton ball or gauze pad.
- Plaster.
- Sharps disposal container.
- **Do not** use if expiry date on Repatha pre-filled syringe carton has passed.

C Choose your injection site.



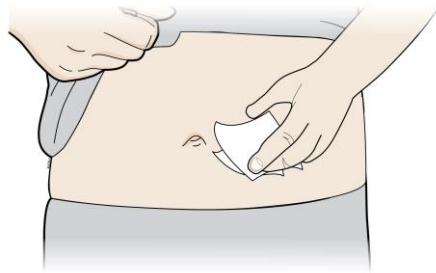
You can use:

- Thigh.
- Belly, except for the 5 centimeters around the belly button.
- Outer area of upper arm (only if someone else is giving you the injections).
- **Do not** choose an area where the skin is tender, bruised, red, or hard. Avoid injecting into areas with scars or stretch marks.



Choose a different site each time you give yourself an injection. If you need to use the same injection site, just make sure it is not the same spot on that site you used last time.

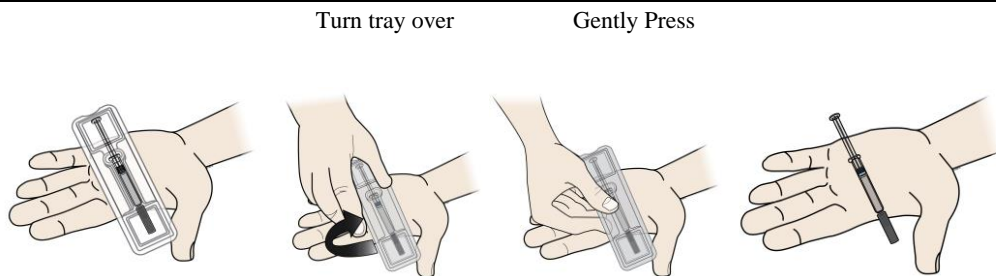
D Clean your injection site.



Clean your injection site with an alcohol wipe. Let your skin dry before injecting.

- **Do not** touch this area of skin again before injecting.

E Remove the pre-filled syringe from the tray.



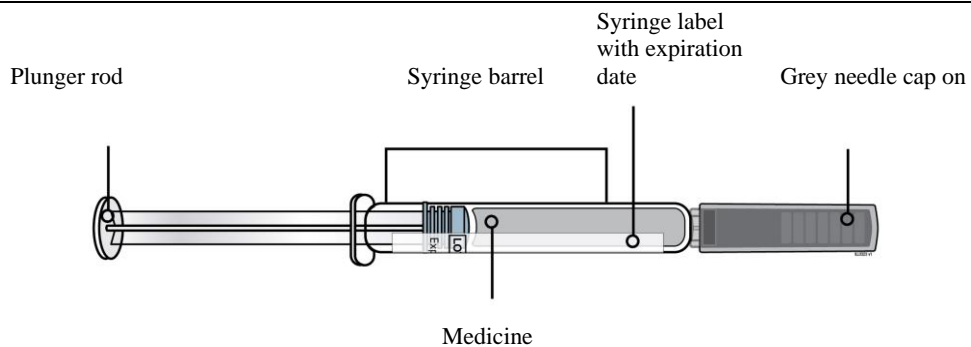
To remove:

- Peel the paper off of the tray.
- Place the tray on your hand.
- Turn the tray over and gently press the middle of the tray's back to release the syringe into your palm.
- If the pre-filled syringe does not release from the tray, gently press on the back of tray.
- **Do not** pick up or pull the pre-filled syringe by the plunger rod or grey needle cap. This could damage the syringe.
- **Do not** remove the grey needle cap from the pre-filled syringe until you are ready to inject.



Always hold the pre-filled syringe by the syringe barrel.

F Inspect medicine and syringe.



Always hold the pre-filled syringe by the syringe barrel.

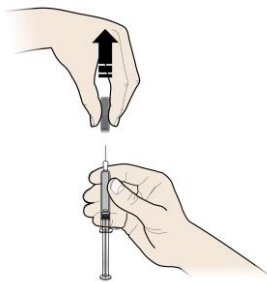
Check that:

- The name Repatha appears on the pre-filled syringe label.
- The medicine in the pre-filled syringe is clear and colorless to slightly yellow.
- **Do not** use the pre-filled syringe if any part of the pre-filled syringe appears cracked or broken.
- **Do not** use the pre-filled syringe if the grey needle cap is missing or not securely attached.
- **Do not** use the pre-filled syringe if the medicine is discolored or contains large lumps, flakes or colored particles.
- **Do not** use the pre-filled syringe if the expiration date on the pre-filled syringe has passed.

Step 2: Get ready

A Carefully pull the grey needle cap straight out and away from your body. Do not leave the grey needle cap off for more than 5 minutes. This can dry out the medicine.

1.



It is normal to see a drop of medicine at the end of the needle.

2.



Immediately place the cap in the sharps disposal container.

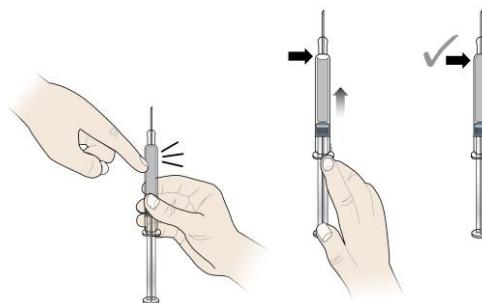
- **Do not** twist or bend the grey needle cap. This can damage the needle.
- **Do not** put the grey needle cap back onto the pre-filled syringe.

B Remove the air bubble/gap.

You may notice an air bubble/gap in the Repatha pre-filled syringe.

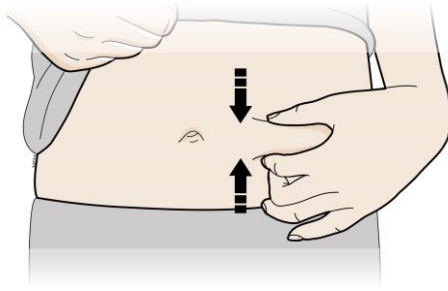
If you notice an air bubble/gap:

- Hold the pre-filled syringe with the needle facing up.
- Gently tap the syringe barrel with your fingers until the air bubble/gap rises to the top of the syringe.
- Slowly and gently push the plunger rod up to get the air out of the pre-filled syringe. Be very careful not to push out any medicine.



- **Do not** tap the syringe needle.

C PINCH your injection site to create a firm surface.



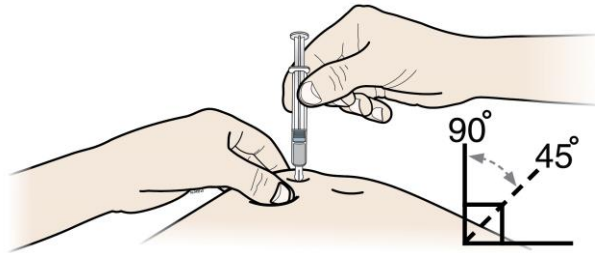
Pinch skin firmly between your thumb and fingers, creating an area about 5 centimeters wide.



It is important to keep the skin pinched while injecting.

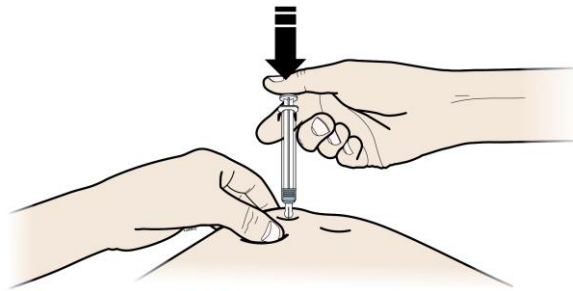
Step 3: Inject

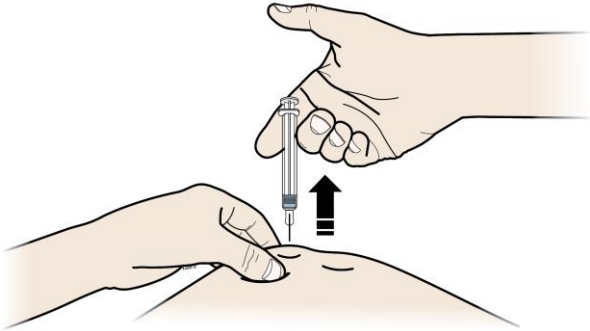
A Hold the PINCH. Insert the needle into the skin using a 45 to 90 degree angle.




- Do not place your finger on the plunger rod while inserting the needle.

B Using slow and constant pressure, PUSH the plunger rod all the way down until the syringe is empty.



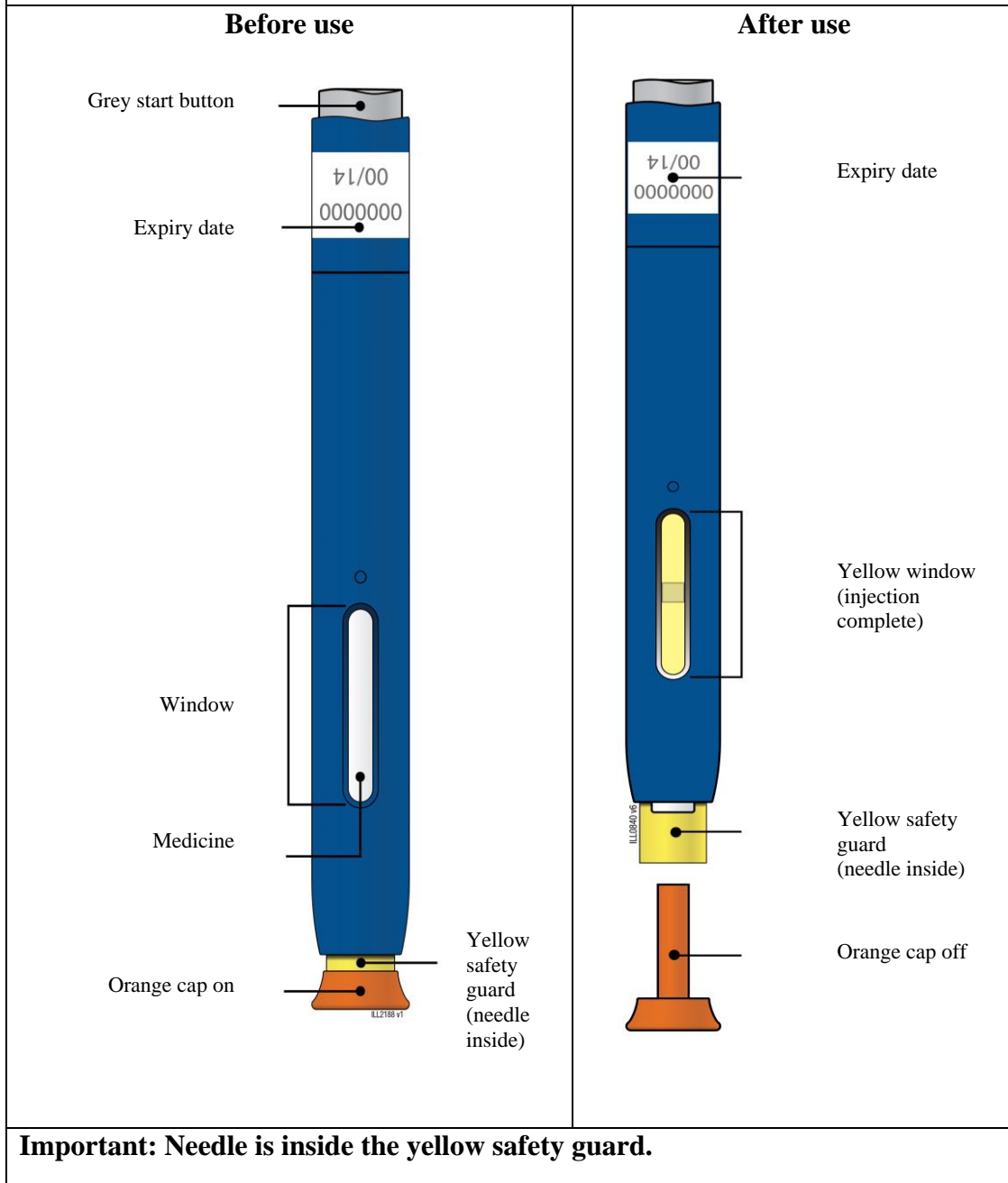
C	When done, RELEASE your thumb, and gently lift the syringe off skin.
	
<ul style="list-style-type: none"> • Do not put the grey needle cap back onto the used syringe. 	

Step 4: Finish	
A	Immediately place the used syringe in a sharps disposal container.
	
<p>Talk with your healthcare provider about proper disposal. There may be local guidelines for disposal.</p> <ul style="list-style-type: none"> • Do not reuse the used syringe. • Do not use any medicine that is left in the used syringe. • Do not recycle the syringe or the sharps disposal container or throw it into household rubbish. <p>! Keep the used syringe and sharps container out of the sight and reach of children.</p>	

B	Examine the injection site.
<p>If there is blood, press a cotton ball or gauze pad on your injection site. Apply a plaster if needed.</p> <ul style="list-style-type: none"> • Do not rub the injection site. 	

Instructions for use:
 Repatha single-use SureClick pre-filled pen

Guide to parts



Important

Before you use the Repatha pre-filled pen, read this important information:

- **Do not** freeze or use the Repatha pre-filled pen if it has been frozen.
- **Do not** remove the orange cap from the Repatha pre-filled pen until you are ready to inject.

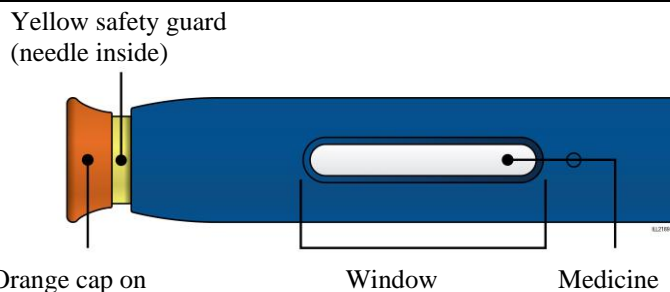
- **Do not** use the Repatha pre-filled pen if it has been dropped on a hard surface. Part of the Repatha pre-filled pen may be broken even if you cannot see the break.

Step 1: Prepare

A Remove one Repatha pre-filled pen from the package.

1. Carefully lift the pre-filled pen straight up out of the box.
 2. Put the original package with any unused pre-filled pens back in the refrigerator.
 3. Wait at least 30 minutes for the pre-filled pen to naturally reach room temperature before injecting.
- **Do not** try to warm the pre-filled pen by using a heat source such as hot water or microwave.
 - **Do not** leave the pre-filled pen in direct sunlight.
 - **Do not** shake the pre-filled pen.
 - **Do not** remove the orange cap from the pre-filled pen yet.

B Inspect the Repatha pre-filled pen.



Make sure the medicine in the window is clear and colorless to slightly yellow.

Check the expiration date.

- **Do not** use the pre-filled pen if medicine is cloudy or discolored or contains large lumps, flakes, or particles.
- **Do not** use the pre-filled pen if any part appears cracked or broken.
- **Do not** use if the pre-filled pen has been dropped.
- **Do not** use the pre-filled pen if the orange cap is missing or not securely attached.
- **Do not** use the pre-filled pen if the expiration date has passed.

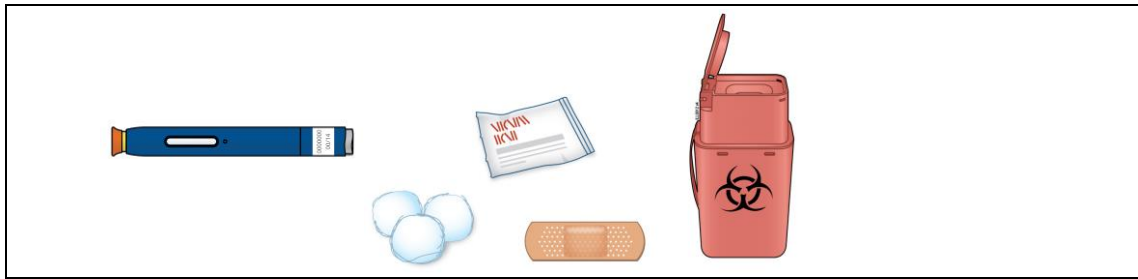
In all cases, use a new pre-filled pen.

C Gather all materials needed for your injection.

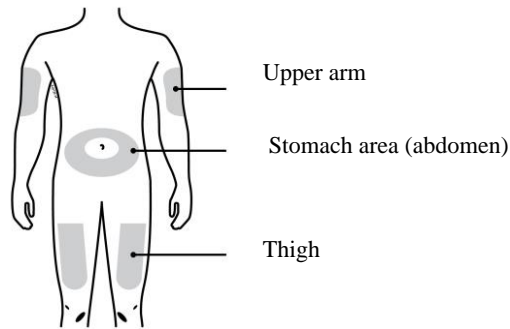
Wash your hands thoroughly with soap and water.

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

- New pre-filled pen.
- Alcohol wipes.
- Cotton ball or gauze pad.
- Plaster.
- Sharps disposal container.



D Prepare and clean your injection site.



Only use these injection sites:

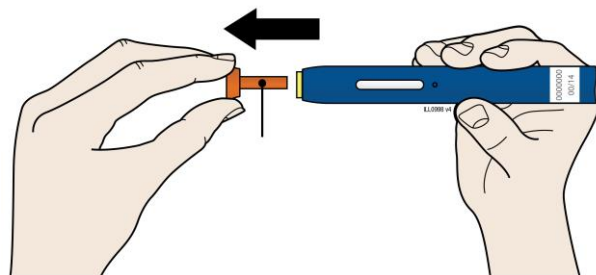
- Thigh.
- Stomach area (abdomen), except for a 5 centimeter area around your belly button.
- Outer area of upper arm (only if someone else is giving you the injection).

Clean the injection site with an alcohol wipe. Let your skin dry.

- **Do not** touch this area again before injecting.
- Choose a different site each time you give yourself an injection. If you need to use the same injection site, just make sure it is not the same spot on that site you used last time.
- **Do not** inject into areas where the skin is tender, bruised, red, or hard. Avoid injecting into areas with scars or stretch marks.

Step 2: Get ready

A Pull the orange cap straight off, only when you are ready to inject. Do not leave the orange cap off for more than 5 minutes. This can dry out the medicine.



Orange cap

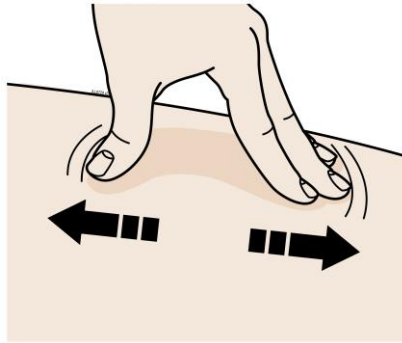
It is normal to see a drop of liquid at the end of the needle or yellow safety guard.

- **Do not** twist, bend or wiggle the orange cap.
- **Do not** put the orange cap back onto the pre-filled pen.
- **Do not** put fingers into the yellow safety guard.

Important: Do not remove the orange cap from the pre-filled pen until you are ready to inject. If you are unable to inject, please contact your healthcare provider.

B	Create a firm surface at the selected injection site (thigh, stomach, or outer areas of the upper arm), by using either the stretch method or the pinch method.
----------	---

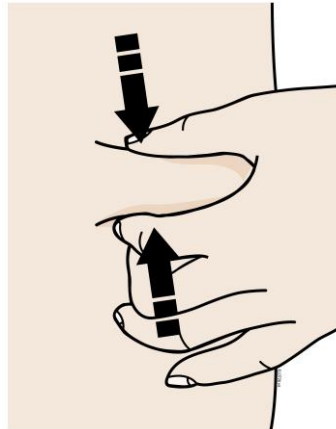
Stretch method



Stretch the skin firmly by moving your thumb and fingers in the opposite direction, creating an area about 5 centimeters wide.

OR

Pinch method



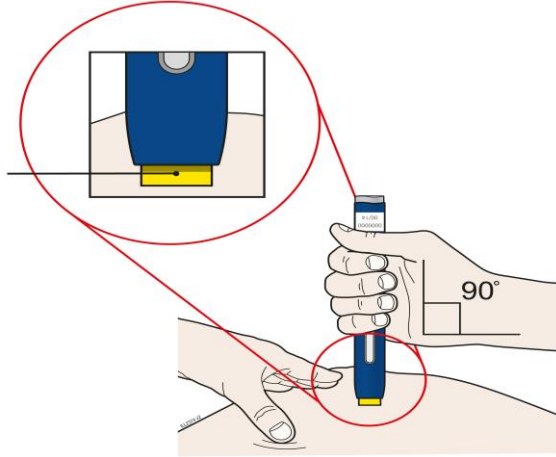
Pinch the skin firmly between your thumb and fingers, creating an area about 5 centimeters wide.

Important: It is important to keep skin stretched or pinched while injecting.

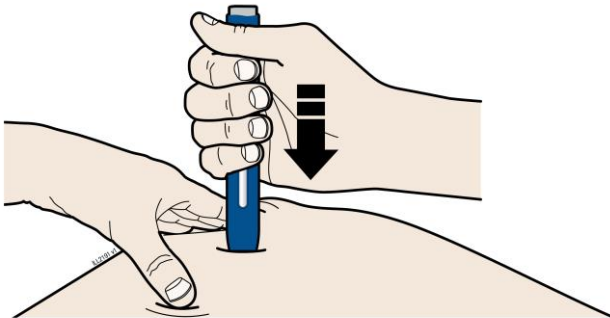
Step 3: Inject

- A** Keep holding the stretched or pinched skin. With the orange cap off, **put** the yellow safety guard on your skin at 90 degrees. The **needle is inside** the yellow safety guard.
Do not touch the grey start button yet.

Yellow safety guard
(needle inside)

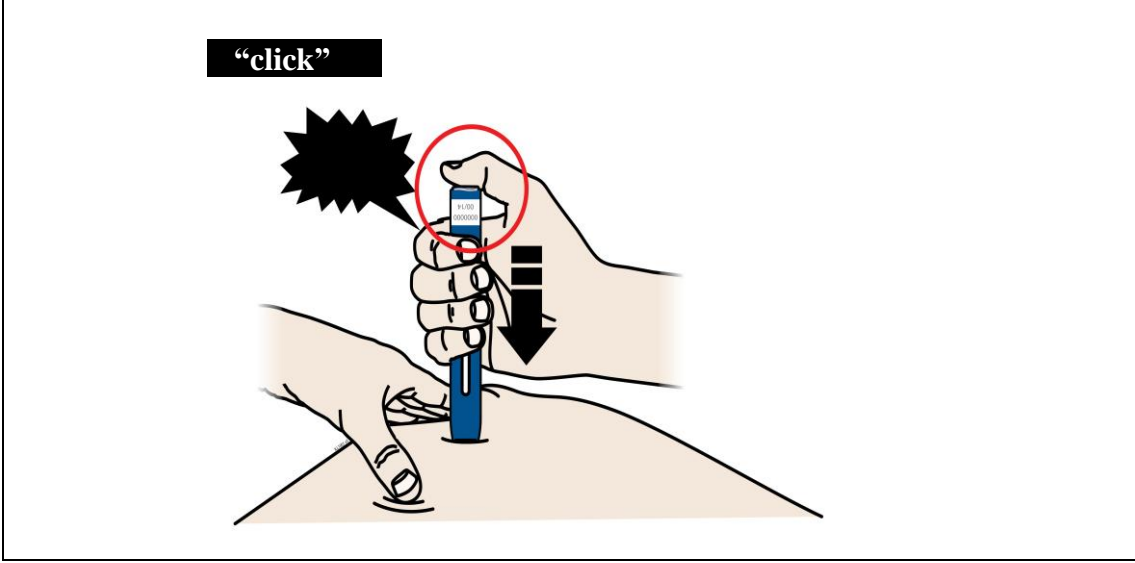


- B** Firmly **push** down the pre-filled pen onto the skin until it stops moving.

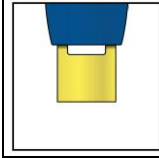
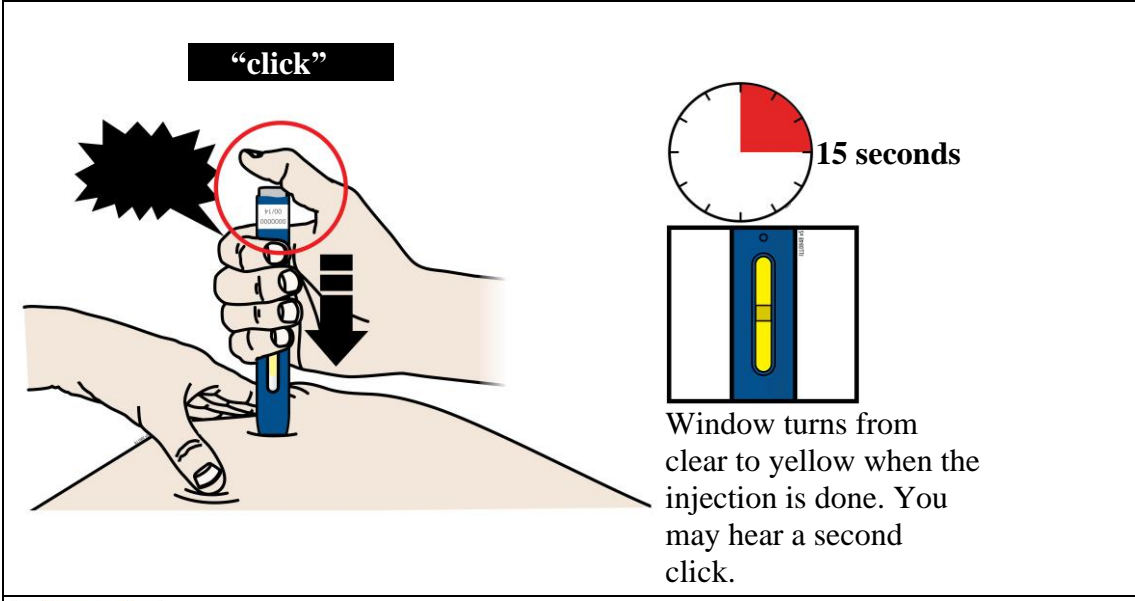


Important: You must push all the way down but **do not** touch the grey start button until you are ready to inject.

C When you are ready to inject, **press** the grey start button. You will hear a **click**.



D Keep **pushing** down on the skin. Then **lift** your thumb while still holding the pre-filled pen on your skin. Your injection could take about 15 seconds.



NOTE: After you remove the pre-filled pen from your skin, the needle will be automatically covered.

Step 4: Finish

A Discard the used pre-filled pen and orange needle cap.



Discard the used pre-filled pen and the orange cap in a sharps disposal container.

Talk with your healthcare provider about proper disposal. There may be local guidelines for disposal.

Keep the pre-filled pen and the sharps disposal container out of the sight and reach of children.

- **Do not** reuse the pre-filled pen.
- **Do not** recap the pre-filled pen or put fingers into the yellow safety guard.
- **Do not** recycle the pre-filled pen or sharps disposal container or throw them into household rubbish.

B Examine the injection site.

If there is blood, press a cotton ball or gauze pad on your injection site. **Do not** rub the injection site. Apply a plaster if needed.