

Package leaflet: Information for the user

Besremi 250 micrograms/0.5 mL solution for injection in pre-filled pen ropeginterferon alfa-2b

▼ 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 taking 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.

What is in this leaflet

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

1. What Besremi is and what it is used for

Besremi contains the active substance ropeginterferon alfa-2b, which belongs to the class of medicinal products called interferons. Interferons are produced by your immune system to block the growth of cancer cells.

Besremi is used as monotherapy for the treatment of polycythaemia vera in adults. Polycythaemia vera is a type of cancer in which the bone marrow produces too many red blood cells, white blood cells and platelets (cells that help the blood to clot).

2. What you need to know before you use Besremi

Do not use Besremi

- if you are allergic to ropeginterferon alfa-2b or any of the other ingredients of this medicine (listed in section 6).
- if you have thyroid disease that is not controlled with medicines.
- if you have or had severe mental disorders (such as depression or suicidal thoughts or if you tried to kill yourself).
- if you have recently had severe heart problems (such as heart attack or stroke)
- if you have or had an autoimmune disease (such as rheumatoid arthritis, psoriasis or inflammatory bowel disease).
- if you had an organ transplantation and you take medicines which suppress your immune system.
- if you take telbivudine (a medicine used to treat hepatitis B infection).
- if you have advanced, uncontrolled liver disease.
- if you have severe kidney disease (with your kidneys working at less than 15% of their normal ability).

Warnings and precautions

Talk to your doctor before using Besremi:

- if you have thyroid disease.
- if you have diabetes or high blood pressure – your doctor may ask you to have an eye examination.
- if you have liver problems – you will have blood tests regularly to check how your liver is working if you are on a long-term Besremi therapy.
- if you have kidney problems.
- if you have psoriasis or other skin problems because they may get worse during treatment with Besremi.

Once you have started Besremi treatment, talk to your doctor:

- if you develop symptoms of depression (such as feelings of sadness, dejection, and suicidal thoughts).
- if you develop signs of a severe allergic reaction (such as difficulty in breathing, wheezing or hives) while using Besremi – if this is the case you will need to seek medical help immediately.
- if you develop symptoms of a cold or other respiratory infection (such as difficulty in breathing, cough, fever and chest pain).
- if you have changes in your vision – you must tell your doctor and have an immediate eye examination. Severe eye problems may occur during Besremi therapy. Your doctor will usually check your vision before starting your treatment. If you have health problems which may lead to eye problems such as diabetes or high blood pressure, your doctor should check your vision also during treatment. If your vision worsens, your doctor may decide to discontinue your treatment.

Dental and gum disorders, which may lead to loss of teeth, can occur with interferon medicines. In addition, dry mouth could damage teeth and the lining of the mouth during long-term treatment with Besremi. You should brush your teeth thoroughly twice daily and have regular dental checks.

It will need a certain time to reach your individual optimal dose of Besremi. Your doctor will decide if it is necessary to treat you with another medicine for an early reduction of your blood cell number to prevent blood clots and bleeding.

Children and adolescents

Do not give this medicine to children and adolescents because no information is available on the use of Besremi in this age group.

Other medicines and Besremi

Tell your doctor or pharmacist if you are using, have recently used or might use any other medicines.

Do not use Besremi if you are taking telbivudine (for treating hepatitis B) since the combination of these medicines increases the risk of peripheral neuropathy (numbness, tingling, or burning sensations in the arms and legs). Tell your doctor if you are being treated with telbivudine.

Tell your doctor especially if you are taking any of the following medicines:

- theophylline (a medicine used to treat respiratory diseases such as asthma)
- methadone (a medicine used to treat pain or opioid dependence)
- vortioxetine or risperidone (medicines used to treat mental disorders)
- anti-cancer medicines such as those stopping or slowing the growth of blood-forming cells in the bone marrow (e.g. hydroxycarbamide)
- medicines that work on the central nervous system to relieve pain, help you sleep, or have a calming effect (e.g. morphine, midazolam)

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine.

Pregnancy

The effect of Besremi during pregnancy is not known. The use of Besremi is not recommended during pregnancy. If you are a woman of childbearing potential, your doctor will discuss with you if effective birth control should be used during your treatment with Besremi.

Breast-feeding

It is not known if Besremi is present in breast milk. Your doctor will help you decide if you have to stop breast-feeding when you are using this medicine.

Driving and using machines

Do not drive or use machines if you feel dizzy, sleepy or confused while using Besremi.

Besremi contains benzyl alcohol

This medicine contains 5 mg benzyl alcohol in each 0.5 mL. Benzyl alcohol may cause allergic reactions.

Ask your doctor or pharmacist for advice:

- if you are pregnant or breast-feeding.
- if you have a liver or kidney disease.

This is because large amounts of benzyl alcohol can build-up in your body and may cause side effects (called “metabolic acidosis”).

Besremi contains sodium

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

3. How to use Besremi

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

The dose will be set individually for you by your doctor for your condition. The usual starting dose of Besremi is 100 microgram every 2 weeks. Your doctor will then increase your dose stepwise and may adjust your dose during treatment.

Your doctor will reduce your starting dose to 50 micrograms if you have severe kidney problems.

This medicine is for subcutaneous use which means that it is injected in the tissue under your skin. It should not be injected into an area of the body where the skin is irritated, reddened, bruised, infected, or scarred.

If you are injecting this medicine yourself, you will get clear instructions on how to prepare and inject it.

To prevent passing on infectious diseases, you should never share Besremi pre-filled pen with anyone else, even when the needle is changed.

Details on how to prepare and inject Besremi are given in the Instructions for Use. Read them before you start using Besremi.

If you use more Besremi than you should

Tell your doctor as soon as possible.

If you forget to use Besremi

You should inject the dose as soon as you remember. However, if more than 2 days have passed since you missed the dose, leave out the dose and inject the next dose when it is due. Do not inject a double dose to make up for a forgotten dose. Check with your doctor or pharmacist if you are not sure.

If you stop using Besremi

Do not stop using Besremi before you have talked to your doctor.

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

4. Possible side effects

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

Contact your doctor immediately if you notice any of the following serious side effects during your treatment with Besremi:

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

- changes in your heartbeat (when the heart beats very fast and uneven)

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

- attempted suicide, thoughts about killing yourself
- loss of vision which may be caused by bleeding in the retina (the retina is the light-sensitive layer in the eye), or by build-up of fat in or under the retina

Rare side effects (may affect up to 1 in 1,000 people):

- loss of vision which may be caused by damage to the retina (such as obstruction of the blood vessels in the eye) or the optic nerve

Very rare side effects (may affect up to 1 in 10,000 people):

- blindness
- breathing problems including shortness of breath, cough and chest pain which may be caused by lung infiltration, pneumonia (lung infection), pulmonary arterial hypertension (high blood pressure in the blood vessels bringing blood from the heart to the lungs) and pulmonary fibrosis (a lung disease where scars are formed in the lung tissue)

Side effects with frequency not known (cannot be estimated from the available data):

- detachment of the retina (you may experience eye problems including changes in vision)

Other side effects

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

- decrease in the number of a type of white blood cells (called leucocytes) and in blood clotting cells (called platelets)
- joint or muscle pain
- flu-like symptoms, feeling tired
- in blood tests: increase of an enzyme called gamma-glutamyltransferase

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

- infection of the respiratory tract, runny or stuffy nose, fungal infections, flu
- decrease in the number or size of red blood cells
- increase or decrease in the thyroid gland activity, increase of thyroid stimulating hormone, inflammation of the thyroid gland
- increase of triglycerides (a type of lipid) in the blood, decreased appetite
- aggressive behaviour, feeling depressed, feeling anxious, problems with falling asleep or staying asleep, mood changes, lacking bodily energy or motivation
- headache, feeling dizzy, reduced sense of touch or sensation, feeling sleepy, sensation of tingling and 'pins and needles'
- dry eyes
- damage of the capillaries (very small blood vessels) in the body

- breathing problems
- diarrhoea, nausea, abdominal pain or stomach discomfort, constipation, dry mouth
- liver disorder, increase in certain liver enzymes (shown in blood tests)
- itching, hair loss, rash, redness of skin, psoriasis, dry and scaly skin, acne, thickening of the outer layer of the skin, increased sweating
- a disorder called Sjogren's syndrome where the body's immune system attacks glands that produce fluid (such as the tear and saliva glands), arthritis, pain in arms and legs, bone pain, painful sudden tightening of a muscle
- fever, weakness, chills, general health problems, irritation or redness at the site of injection, decreasing body weight
- in blood tests: antibodies which are produced by the body's immune system, increase of an enzyme called lactate dehydrogenase

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

- infection and re-infection with herpes, bacterial infections
- increase in the number of platelets
- autoimmune disorder of the thyroid gland, sarcoidosis (areas of inflamed tissue in different parts of the body)
- diabetes
- panic attack, hallucination (seeing, hearing or feeling things that are not there), feeling stressed, feeling nervous, lack of interest in activities, nightmare, irritability, confusion
- damage to the nervous system, migraine, mental disorder (health condition involving changes in thinking, emotion or behaviour), visual or sensory disturbances, shaky hands
- eye discomfort, eyelid eczema
- hearing loss, ringing in ears (tinnitus), spinning feeling (vertigo)
- heart disorders such as heart block (a disorder in the heart's electrical activity), blood clots in the blood vessels of the heart, leakage of the aortic valve
- high blood pressure, reduced blood supply to certain parts of the body, haematoma (collection of blood under the skin), flushing
- inflammation of lung tissue, coughing, nosebleed, sore throat
- inflammation of the stomach, abdominal wall disorder, intestinal gas, indigestion, painful swallowing, bleeding gums
- inflammation of the liver, damage to the liver, enlarged liver
- sensitivity to sunlight, peeling of the skin, nail disorder
- muscle weakness, neck pain, groin pain
- inflammation of the bladder, painful urination, increased need to urinate, inability to urinate
- sexual problems
- pain or itching at the site of injection, sensitivity to weather change
- non-acute porphyria (a liver disorder in which substances called porphyrins build up in the skin causing local skin damage, such as rashes, blisters, sores or discomfort, upon sun exposure)
- in blood tests: increase of uric acid, antibodies produced by the body's immune system against red blood cells

Rare side effects (may affect up to 1 in 1,000 people):

- bipolar disorders (mood disorders with episodes of sadness and excitement), mania (extreme excitement or unreasonable enthusiasm)
- cardiomyopathy (diseases that affect the heart muscle), angina pectoris (a severe chest pain as a result of blockage of the heart vessels)
- liver failure

Very rare side effects (may affect up to 1 in 10,000 people):

- idiopathic or thrombotic thrombocytopenic purpura (increased bruising, bleeding, decreased platelets, anaemia and extreme weakness)
- myocardial ischemia (reduced blood flow to your heart muscle)

Side effects with frequency not known (cannot be estimated from the available data):

- Vogt-Koyanagi-Harada disease (a rare disease that can lead to loss of vision, hearing and skin pigmentation), severe allergic reaction
- discolouration of the skin
- periodontal (affecting gums) and dental disorders, change in colour of the tongue

Reporting of side effects

If you get any side effects, talk to your doctor, pharmacist, or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via Yellow Card Scheme Website: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Besremi

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 the outer 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.

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

Once opened, the pre-filled pen may be stored for a maximum of 30 days in the refrigerator (2 °C - 8 °C) when stored with the pen cap on and kept in the outer carton in order to protect from light.

Do not use this medicine if you notice that the pre-filled pen appears damaged, the solution is cloudy, has particles or flakes, or has any colour other than colourless to slightly yellow.

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 Besremi contains

- The active substance is ropeginterferon alfa-2b.
Each pre-filled pen of 0.5 mL solution contains 250 micrograms of ropeginterferon alfa-2b as measured on a protein basis, corresponding to 500 micrograms/mL.
- The other ingredients are sodium chloride, polysorbate 80, benzyl alcohol, anhydrous sodium acetate, glacial acetic acid, and water for injections. For benzyl alcohol and sodium, see section 2 “Besremi contains benzyl alcohol” and “Besremi contains sodium”.

What Besremi looks like and contents of the pack

Besremi is presented as a solution for injection (injection) in a pre-filled pen. Each pre-filled pen contains 0.5 mL of solution. It is available in packs containing 1 pre-filled pen and 2 injection needles (Type: mylife Clickfine 8mm)

Marketing Authorisation Holder and Manufacturer

AOP Orphan Pharmaceuticals GmbH
Leopold-Ungar-Platz 2
1190 Vienna
Austria

This leaflet was last revised in February 2023.

Instructions for Use

Please read this leaflet carefully before using the Besremi 250 micrograms pre-filled pen. If you have any further questions, ask your doctor or pharmacist.

Your doctor or pharmacist will show you how to use the pen.

The Besremi 250 micrograms pre-filled pen can be used to inject doses of 50, 100, 150, 200 and 250 micrograms. At doses up to 100 micrograms, the same pen can be used twice. Your doctor will tell you the dose you need. Please note down your injection dates and dose as instructed by your doctor.

If you need a dose of more than 250 micrograms, you require two Besremi 250 microgram pre-filled pens. You must use a different injection site for each of the two pens. Your doctor or pharmacist will explain to you how to use the two pens.

Store the pen in the outer carton in the refrigerator.

Remove the pen from the refrigerator 15 minutes before the injection to let it reach room temperature. Find a quiet and well-lit area for the injection.

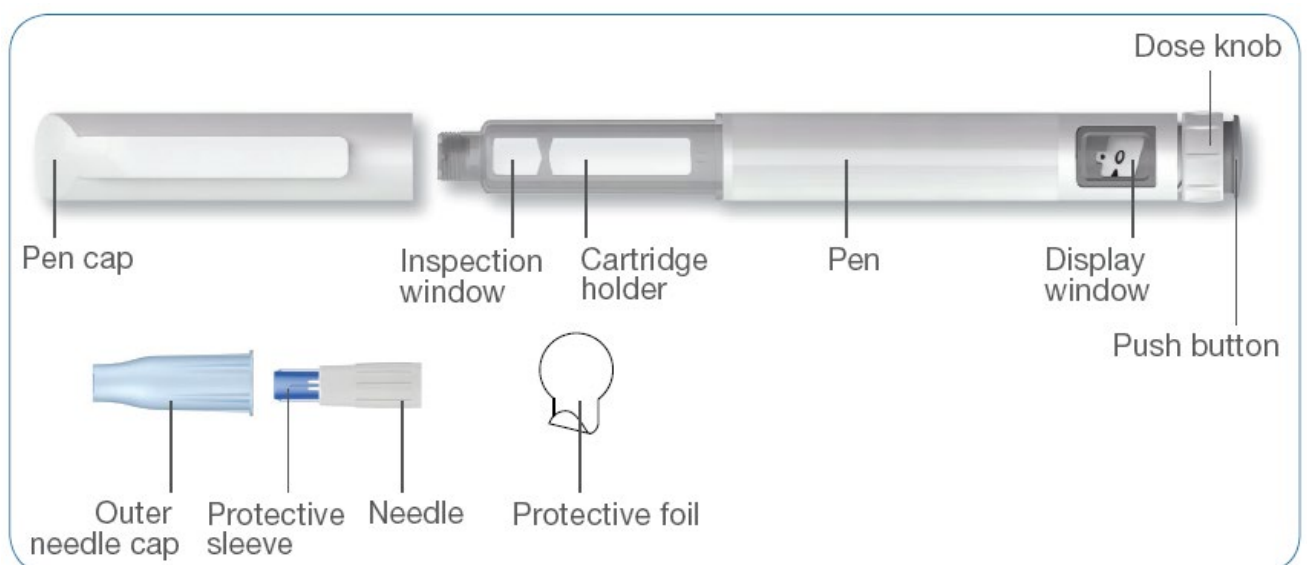
You will need the following supplies for your injection:

- Besremi pre-filled pen
- Needle (Type: mylife Clickfine 8mm)
- Alcohol wipe (not supplied)
- Optional: adhesive plaster (not supplied)

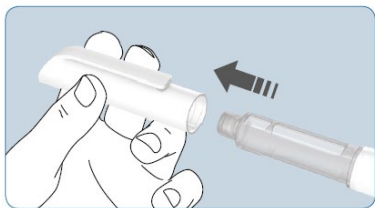
The Besremi pre-filled pen comes with two or six needles (depending on the pack-size). Always use a new needle for each injection.

Do not use the pen if it appears damaged. If at any time during the use of the pen, you feel you may have damaged it (e. g. by dropping it or using excessive force), do not continue to use the pen. Get a new pen and start over.

Description Besremi 250 micrograms pre-filled pen

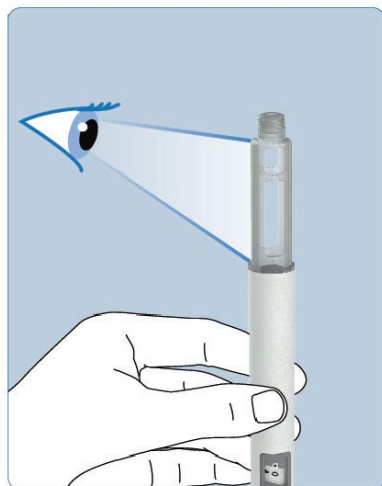


1



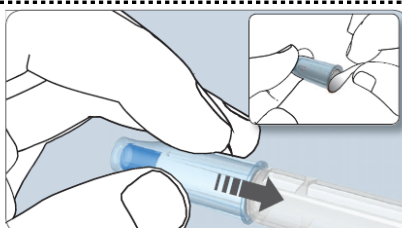
- Wash your hands before using Besremi.
- Check that the product has not expired.
- Remove the cap from the pen.

2



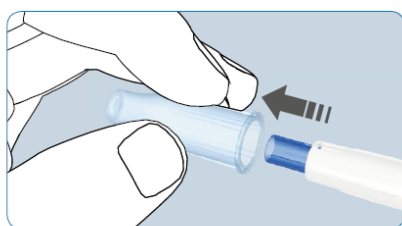
- Check the solution through the inspection windows along the sides of the cartridge holder.
- Do not use the pen if the solution is cloudy, has particles or flakes, or is any colour other than colourless to slightly yellow.

3



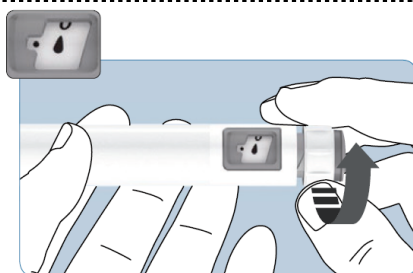
- Take a new needle and remove the protective foil.
- Place the needle with the outer needle cap straight and centrally arranged onto the pen to prevent it from buckling or bending.
- Make sure that it is firmly attached.

4



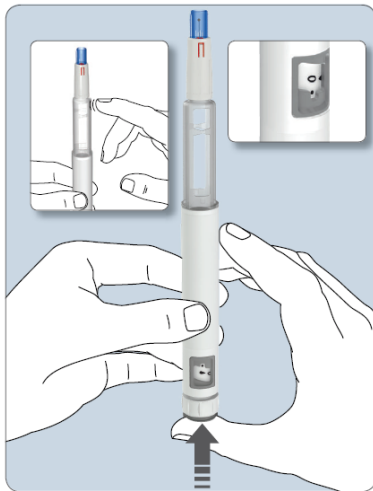
- Remove the outer needle cap from the needle.
- Do not put the outer needle cap back on the needle until you have injected the medicine. Do not touch the needle tip at any time.
- If you have used your Besremi 250 microgram pre-filled pen once before and are using it a second time, continue directly with step 7.
- If you are using this pen for the first time, continue with preparation of the pen in step 5.

5



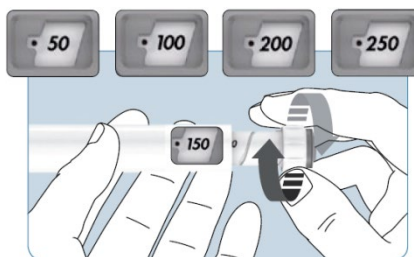
- If you are using this pen for the first time, prepare the pen for injection by turning the dose knob until you see the icon of a “drop” and the dot in the window. The icon of a “drop” must be aligned with the dot in the display window.

6



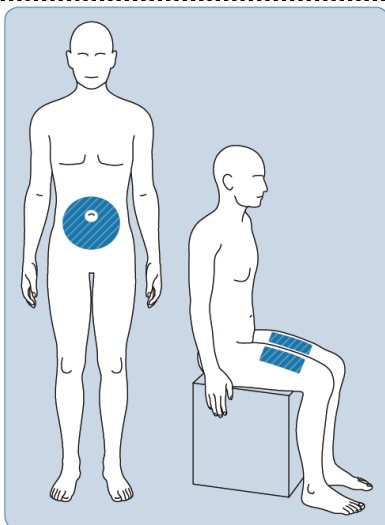
- Hold the pen with the needle pointing upwards and make sure the display window is facing you.
- Do not point towards your face or anyone else's face.
- Tap the pen (cartridge holder) gently with your fingers to allow any air bubbles to rise to the top of the cartridge holder.
- Press the push button with your thumb until the "0" mark is aligned with the dot in the display window.
- You will see the window changes between the "drop" icon and the "0" mark, and you will hear gentle clicks when the button moves.
- You should see a droplet of liquid appearing at the needle tip.
- If you do not see a droplet at the needle tip, repeat steps 5 and 6 up to six times until a droplet appears.
- If you do not see the droplet after the seventh time, ask your doctor or pharmacist for advice.

7



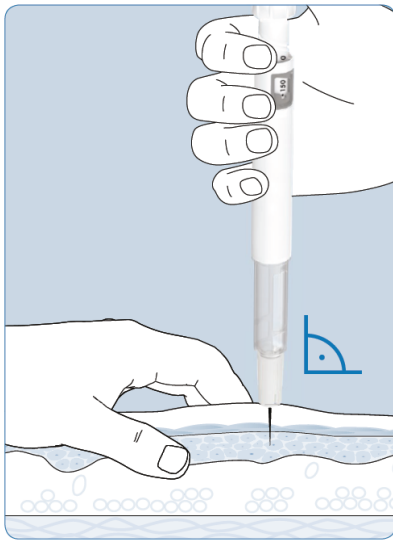
- Set the dose your doctor advised by turning the dose knob until the prescribed dose is visible. The selected dose must align with the dot and dose display window. If necessary, correct the dose by turning the dose knob.
- If you are unable to reach the required dose setting by turning the dose knob, your pen may be out of sufficient medicine. Do not use any further force. Instead, get a new pen.

8



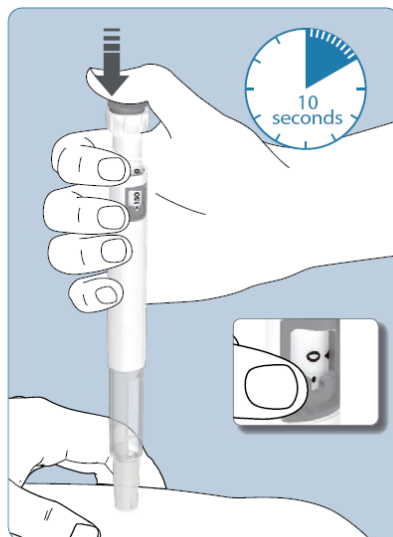
- Disinfect your skin in the injection area using an alcohol swab before the injection.
- Let the area dry before you inject the medicine.
- You must inject the medicine subcutaneously (under the skin). Your doctor will tell you where you must inject it.
- Possible injection sites are the belly (more than five centimetres away from the belly button) or the thigh.
- If you need two pens, use a different injection site for each pen (e. g. right and left side of belly or right and left thigh).
- Do not inject into irritated, reddened, bruised, infected or scarred skin in any way.

9



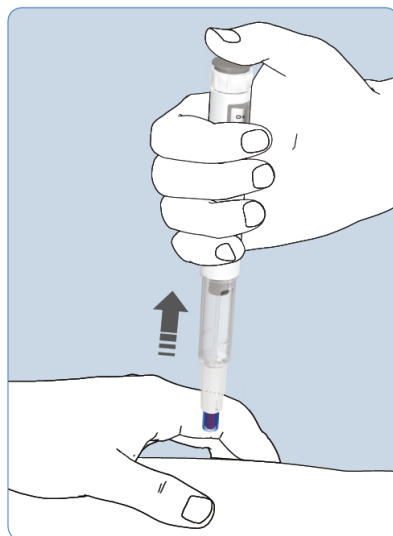
- Hold the pen so that the display window and the label are visible during the injection.
- Raise a fold of skin between the thumb and forefinger.
With gentle pressure insert the needle at a 90 degrees angle until the blue protective sleeve on the needle is no longer visible.

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- Press the push button all the way down until the “0” mark is aligned with the dot in the display window.
- The soft clicking sounds will stop when the injection is complete.
- Hold down the push button and wait at least 10 seconds before removing the needle. Do not lift or move the pen during injection.

11

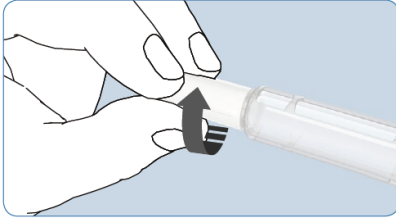


- Carefully remove the needle from the skin.
- Keep the injection site clean until the small injection wound has closed. Apply an adhesive plaster if needed.

Note:

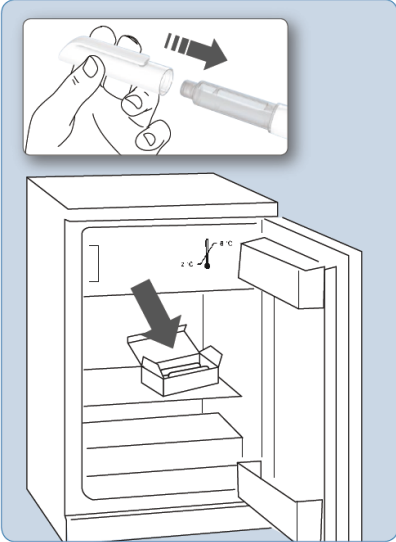
- The blue protective sleeve locks automatically and the now visible red locking indicator covers the needle for your protection. If this is not the case, please ask your doctor or pharmacist.
- After removing the needle, a small droplet of liquid may remain on your skin. This droplet is normal and does not mean that you underdosed.

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- Unscrew the needle and dispose of it properly.
- Put the cap back on the pen securely.

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Reuse of the pen:

- Your doctor will tell you if you may use the pen for a second injection. In this case, put the pen back into the outer carton and store it in the refrigerator for the next use. Do not use the pen after 30 days.

Disposal of the pen and needle:

- Discard the pen and needle after use according to local regulations or as instructed by your doctor or pharmacist.