

PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE
PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986

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

Benlysta S.C. 200 mg

Solution for injection in pre-filled pen

Each 1 ml pre-filled pen contains 200 mg belimumab.

For the list of the inactive and allergenic ingredients in the medicine, see section 2 - "Important information about some of the ingredients in the medicine" and section 6 - "Additional information".

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the physician or 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.

1. WHAT IS THE MEDICINE INTENDED FOR?

Benlysta Subcutaneous 200 mg is indicated as an add-on therapy in adult patients with active, autoantibody-positive systemic lupus erythematosus (SLE) with a high degree of disease activity (e.g., positive anti-dsDNA and low complement) despite standard therapy.

Benlysta, in combination with immunosuppressive therapies, is intended for the treatment of adult patients with active lupus nephritis.

Therapeutic group: selective immunosuppressant.

Lupus is a disease in which the immune system (the system that fights infection) attacks your own cells and tissues, causing inflammation and organ damage. The disease can affect almost any organ in the body, and is thought to involve a type of white blood cells called B cells.

Benlysta S.C. 200 mg contains **belimumab** (a human monoclonal antibody). It

reduces the number of B cells in your blood by blocking the action of BLyS, a protein that helps B cells live longer and is found in high levels in people with lupus.

You will be given Benlysta S.C. 200 mg in addition to your usual treatment for lupus.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- you are sensitive (allergic) to belimumab or to any of the additional ingredients contained in this medicine (listed in section 6).
- **Tell your physician** if you think any of these may apply to you.

Special warnings regarding use of the medicine

Before the treatment with Benlysta S.C. 200 mg, tell the physician if:

- you have a current or **long-term infection** or if you often get infections. Your physician will decide if you can be given Benlysta S.C. 200 mg.
 - you are **planning to get vaccinated or were vaccinated** within the last 30 days. Some vaccines should not be given just before or during treatment with Benlysta S.C. 200 mg.
 - your lupus **affects your nervous system**.
 - if you are **HIV positive** or have **low immunoglobulin** levels.
 - you have, or have had, hepatitis **B or C**.
 - you have had an **organ transplant**, or a **bone marrow** or **stem cell transplant**.
 - you have had **cancer**.
- **Tell your physician** if any of these may apply to you.

Depression and suicide

There have been reports of depression, suicidal thoughts, and suicide attempts including suicide during treatment with Benlysta. Tell your physician if you have a history of these conditions. If you experience new or worsening symptoms at any time:

→ **Contact your physician or go to a hospital straight away.**

If you feel depressed or have thoughts of harming yourself or committing suicide, you may find it helpful to tell a relative or close friend and ask them to read this leaflet. You might ask them to tell you if they are worried about changes in your mood or behavior.

Look out for important symptoms

Patients taking medicines that affect their immune system may be more at risk of contracting infections, including a rare but serious brain infection called progressive multifocal leukoencephalopathy (PML).

→ For further information, read “Increased risk of brain infection” in section 4 of this leaflet.

Children and adolescents

Do not give Benlysta S.C. 200 mg to children or adolescents under 18 years of age.

Drug interactions

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the physician or pharmacist. Especially if you are taking medicines that affect the immune system, including any medicine that affects your B cells (to treat cancer or inflammatory diseases).

→ Using such medicines in combination with Benlysta S.C. 200 mg may make your immune system less effective. This could increase your risk of a serious infection.

Pregnancy and breast-feeding

Contraceptives in women of child-bearing potential

Use an effective method of contraception during treatment with Benlysta S.C. 200 mg and for at least 4 months after the last dose.

Pregnancy

Benlysta S.C. 200 mg is not usually recommended if you are pregnant.

- Tell your physician if you are pregnant, think you may be pregnant, or are

planning to become pregnant. Your physician will decide if you can use Benlysta S.C. 200 mg.

- **If you become pregnant while being treated with Benlysta S.C. 200 mg, tell your physician.**

Breast-feeding

Tell your physician if you are breast-feeding. It is likely that Benlysta S.C. 200 mg can pass into breast milk. Your physician will discuss with you whether you should stop treatment with Benlysta S.C. 200 mg while you are breast-feeding, or if you should stop breast-feeding.

Driving and using machines

Benlysta S.C. 200 mg can cause side effects which may impair your ability to drive or use machinery.

Important information about some of the ingredients in the medicine

Important information about the contents of Benlysta:

Benlysta S.C. 200 mg contains less than 1 mmol sodium (23 mg) per dose, so it is essentially 'sodium-free'.

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the physician's instructions. Check with the physician or pharmacist if you are uncertain about the preparation dosage and treatment regimen.

Benlysta S.C. 200 mg should be injected under your skin on the same day each week.

The dosage and treatment regimen will be determined by the physician only.

Systemic lupus erythematosus (SLE)

The recommended dosage is usually: 200 mg (complete contents of one pen), once a week.

Lupus nephritis

The recommended dosage may vary. Your physician will prescribe the right dosage for you, which is either:

- a dose of 200 mg (complete contents of one pen) once a week.

or

- a dose of 400 mg (complete contents of two pens in one day) once a week for 4 weeks. After this, the recommended dosage is 200 mg (complete contents of one pen) once a week.

If you wish to change your injection day:

Inject a dose on the new day (even if it is less than a week since your last dose).

Continue with the new weekly schedule from that day.

Injecting Benlysta S.C. 200 mg:

Your nurse or physician will show you or your caregiver how to inject Benlysta S.C. 200 mg. Your first injection with the Benlysta S.C. 200 mg pre-filled pen will be supervised by your nurse or physician. After you have been trained on how to use the pen, your nurse or physician may decide that you can give yourself the injection, or your caregiver can give it to you. Your nurse or physician will also tell you what signs and symptoms to look out for when using Benlysta S.C. 200 mg, because serious allergic reactions can occur (see section 4 “Allergic reactions”).

Benlysta S.C. 200 mg should be injected under the skin in the abdominal or thigh area.

Benlysta S.C. 200 mg is a subcutaneous injection and must not be injected into a vein (I.V.).

Step-by-step instructions for using the pre-filled pen are given at the end of this leaflet.

Do not exceed the recommended dose.

If you accidentally have taken a higher dosage of Benlysta S.C. 200 mg

Refer immediately to a physician or nurse, who will monitor you for any signs

or symptoms of side effects, and treat these symptoms, if necessary. If possible, show them the pack, or this leaflet.

If you took an overdose, or if a child has accidentally swallowed the medicine, refer immediately to a physician or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forgot to take Benlysta S.C. 200 mg

Inject the missed dose as soon as you remember. Then continue with your normal weekly schedule as usual or start a new weekly schedule starting from the day you inject the missed dose.

If you did not notice that you have missed a dose until it is already time for your next dose, just inject the next dose as planned.

Adhere to the treatment regimen recommended by your physician.

Stopping treatment with Benlysta S.C. 200 mg

Even if your health condition improves, do not stop treatment with the medicine without consulting the physician.

Your physician will decide if you need to stop using Benlysta S.C. 200 mg.

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 further questions regarding use of the medicine, consult the physician or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Benlysta S.C. 200 mg may cause side effects in some users. Do not be alarmed by reading the list of side effects. You may not suffer from any of them.

Allergic reactions - refer for medical help immediately

Benlysta S.C. 200 mg can cause a reaction to the injection, or an allergic (hypersensitivity) reaction. These are common side effects (may occur in up to 1 in 10 people). These effects can occasionally be severe (uncommon side effects, may occur in up to 1 in 100 people), and could be life-threatening.

These severe effects are more likely to happen on the day of your first or second treatment with Benlysta S.C. 200 mg, but can be delayed and occur a few days later.

Tell your physician or nurse immediately, or proceed to the emergency room of the nearest hospital, if you experience any of the following symptoms of an allergic or injection-related reaction:

- swelling of the face, lips, mouth or tongue
- wheezing, difficulty in breathing or shortness of breath
- rash
- itchy bumps on the skin or hives.

Rarely, less severe delayed reactions to Benlysta can also occur, usually 5 to 10 days after the injection. They include symptoms such as rash, nausea, tiredness, muscle aches, headaches, or facial swelling.

If you experience these symptoms, particularly if you experience two or more symptoms together:

→ **Tell your physician or nurse.**

Infections

Benlysta S.C. 200 mg can make you more likely to get infections, including infections of the urinary and respiratory tracts. These side effects are very common and may affect more than 1 in 10 people. Some of the infections can be severe and can uncommonly cause death.

If you experience any of the following symptoms of an infection:

- fever and/or chills
- cough, breathing problems
- diarrhea, vomiting
- burning sensation while passing urine; urinating often
- warm, red or painful skin or sores on your body.

→ **Tell your physician or nurse immediately.**

Depression and suicide

There have been reports of depression, suicidal thoughts, and suicide attempts

during treatment with Benlysta. Depression can occur in up to 1 in 10 people, suicidal thoughts and suicide attempts can occur in up to 1 in 100 people. If you feel depressed, have thoughts about harming yourself or other distressing thoughts, or if you are depressed and notice that you feel worse or develop new symptoms:

→ **Contact your physician or go to a hospital straight away.**

Increased risk of brain infection:

Medicines that weaken your immune system, such as Benlysta S.C. 200 mg, may put you at higher risk of getting a rare but serious and life-threatening brain infection called progressive multifocal leukoencephalopathy (PML).

Symptoms of progressive multifocal leukoencephalopathy:

- memory loss
- trouble thinking
- difficulty talking or walking
- loss of vision

→ **Tell your physician immediately** if you experience any of these symptoms, or similar problems that lasted more than several days.

If you already had these symptoms before you started treatment with Benlysta S.C. 200 mg:

→ **Tell your physician immediately** if you notice any changes in these symptoms.

Other possible side effects:

Very common side effects

These may affect **more than 1 in 10** people:

- bacterial infections (see 'Infections' section above)

Common side effects

These may affect **up to 1 in 10** people:

- high temperature or fever
- injection site reactions, for example: rash, redness, itching or swelling of the skin where you have injected Benlysta S.C. 200 mg
- itchy, bumpy rash (hives), skin rash

- low white blood cell count (can be identified in a blood test)
- nose, throat, or stomach infection
- pain in hands or feet
- migraine
- feeling sick, diarrhea

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in this leaflet, consult with the physician.

Reporting side effects

Side effects can be reported to the Ministry of Health by clicking on the link “Report Side Effects of Drug Treatment” found on the Ministry of Health homepage (www.health.gov.it) that directs you to the online form for reporting side effects, or by entering the link:

<https://sideeffects.health.gov.it>

5. HOW TO STORE THE MEDICINE?

- Avoid poisoning! This medicine and any other medicine should be kept in a closed place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the physician.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C to 8°C).
- Do not freeze.
- Store in the original package in order to protect from light.
- Remove from the refrigerator 30 minutes before use.
- The pre-filled pen can be stored at room temperature (up to 25°C) protected from light, for a maximum of 12 hours. Once removed from the refrigerator, **the pen must be used within 12 hours or discarded.**
- Do not discard medicines in the wastewater or household waste bin. Ask the pharmacist how to dispose of medicines that are no longer in use. These measures will help protect the environment.

6. ADDITIONAL INFORMATION

- In addition to the active ingredient, the medicine also contains:
Sodium Chloride, L-Arginine Hydrochloride, L-Histidine Monohydrochloride, L-Histidine, Polysorbate 80, Water for Injection
See section 2 “**Important information about some of the ingredients in the medicine**”
- What the medicine looks like and the contents of the package:
Benlysta S.C. 200 mg is marketed as a single use pre-filled pen that contains 1 ml of a colorless to yellowish solution.
Each pack contains 1 or 4 pre-filled pens.
Not all package sizes may be marketed.
- License Holder: GlaxoSmithKline (Israel) Ltd., 25 Basel St., Petach Tikva.
- Manufacturer: GlaxoSmithKline Trading Services Limited, Dublin, Ireland.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health: 161-25-35439

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Step-by-step instructions for using the pre-filled pen

Once-Weekly

Follow the instructions below on how to use the pre-filled pen correctly.

Failure to follow the instructions may affect proper functioning of the pre-filled pen.

You should also receive training on how to use the pre-filled pen.

Benlysta S.C. 200 mg is for **subcutaneous use only**.

Storage

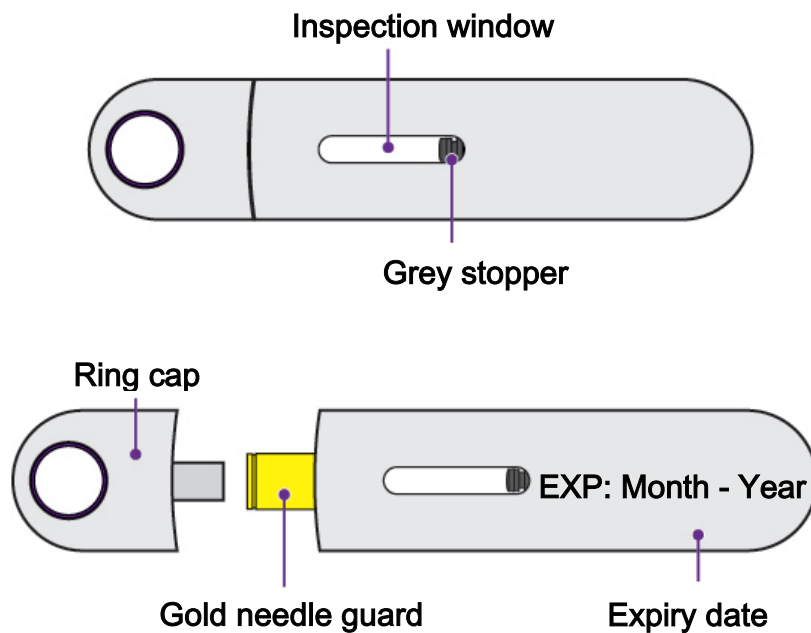
- Store in a refrigerator (between 2°C to 8°C).
- **Do not freeze.**

- Keep in the carton in order to protect from light.
- Remove from the refrigerator 30 minutes before use.
- The pre-filled pen can be stored at room temperature (up to 25°C) protected from light, for a maximum of 12 hours. Once removed from the refrigerator, **it must be used within 12 hours or discarded.**
- Keep out of the reach and sight of children.

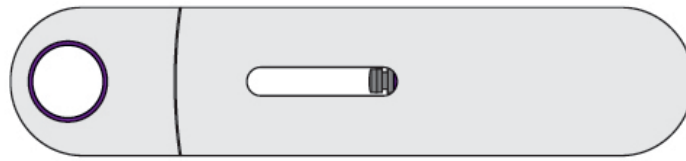
Warnings

- The pre-filled pen is for single use and should be discarded thereafter.
- **Do not** share your Benlysta S.C. 200 mg pre-filled pen with another person.
- **Do not** shake.
- **Do not** use if dropped onto a hard surface.
- **Do not** remove the ring cap until just before the injection.

Benlysta S.C. 200 mg pre-filled pen parts



Supplies needed for the injection



Benlysta S.C. 200 mg pre-filled pen



Alcohol swab

(not included in the pack)



Gauze pad or cotton ball

(not included in the pack)

1. Gather and check supplies

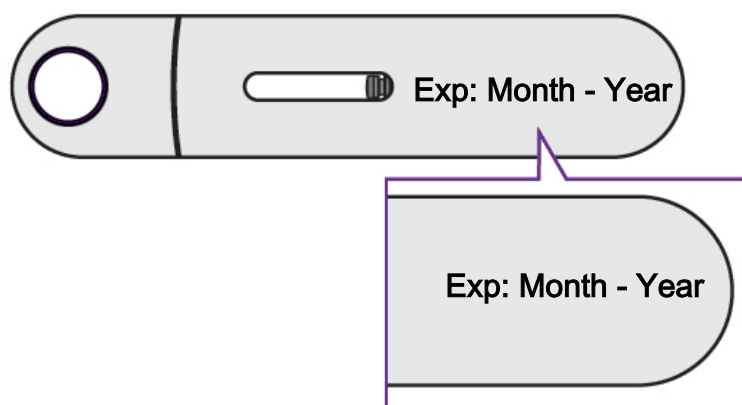
Gather supplies

- Remove from the refrigerator one sealed tray containing a pre-filled pen.
- Find a comfortable, well-lit and clean surface and place the following supplies within reach:
 - Benlysta S.C. 200 mg pre-filled pen.
 - alcohol swab *(not included in the pack)*.
 - gauze pad or cotton ball *(not included in the pack)*.
 - empty container with a tight-fitting lid for pen disposal after use *(not included in the pack)*.
- **Do not** perform the injection if you do not have all the above-listed supplies.

Check the expiry date

- Peel back the cover of the tray and remove the pre-filled pen.
- Check the expiry date on the pre-filled pen (*Figure 1*).

Figure 1



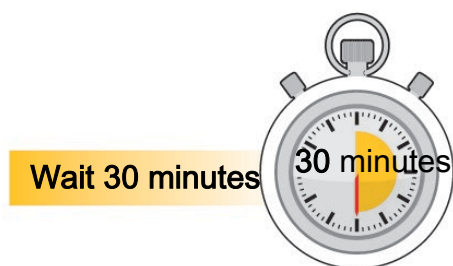
- Do not use the medicine if the expiry date has passed

2. Prepare and inspect the pre-filled pen

Allow the pen to reach room temperature

- Leave the pen at room temperature for 30 minutes (*Figure 2*). Injecting cold Benlysta S.C. 200 mg pen may take longer and may be uncomfortable.

Figure 2



- Do not warm the pen in any other way. For example, do not warm it in a microwave oven, in hot water or in direct sunlight.

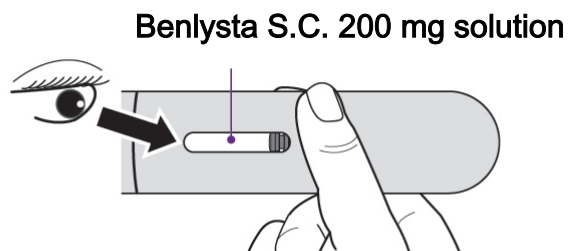
- Do not remove the ring cap during this step.

Inspect the Benlysta S.C. 200 mg solution

- Look in the inspection window to check that the Benlysta S.C. 200 mg solution is colorless to slightly yellow in color (*Figure 3*).

It is normal to see one or more air bubbles in the solution.

Figure 3



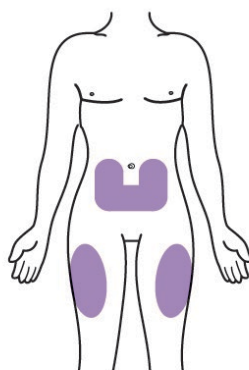
- Do not use if the solution looks cloudy, discolored or has particles.

3. Choose and clean the injection site

Choose the injection site

- Choose the injection site (abdomen or thigh) as seen in *Figure 4*.

Figure 4



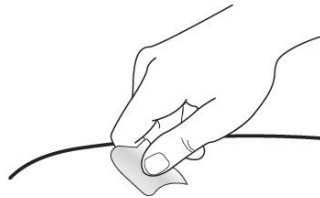
- If you need 2 injections to complete your dose, leave at least 5 cm between each injection if using the same site.

- **Do not** inject into the exact same site each time. This is to prevent the skin from becoming hardened.
- **Do not** inject in areas where the skin is tender, bruised, red or hard.
- **Do not** inject within 5 cm of the navel.

Clean the injection site

- Wash your hands.
- Clean the injection site by wiping it with an alcohol swab (*Figure 5*). Allow the skin to air dry.

Figure 5



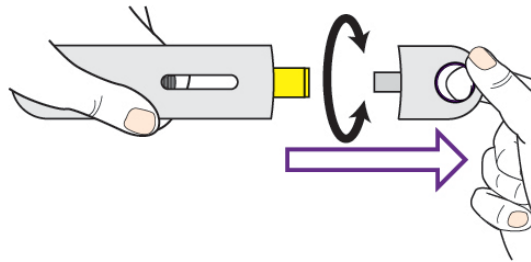
- **Do not** touch this area again before giving the injection.

4. Prepare for the injection

Remove the ring cap

- **Do not** remove the ring cap until immediately before the injection.
- Remove the ring cap by pulling or twisting it off. The ring cap may be twisted off either clockwise or counter-clockwise (*Figure 6*).

Figure 6

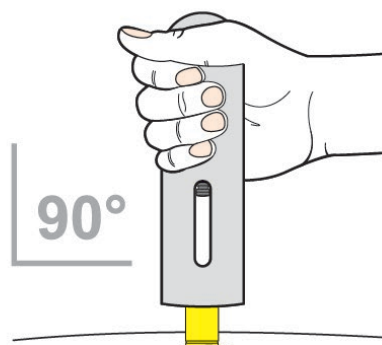


- Do not put the ring cap back onto the pen.

Position the pen

- Hold the pen comfortably so that you can view the inspection window. This is important so that you can confirm administration of a complete dose (*Figure 7*).

Figure 7



- If needed, make the injection site firm by pulling or stretching the skin.
- Position the pen straight over the injection site (at a 90° angle). Make sure the gold needle guard is flat on the skin.

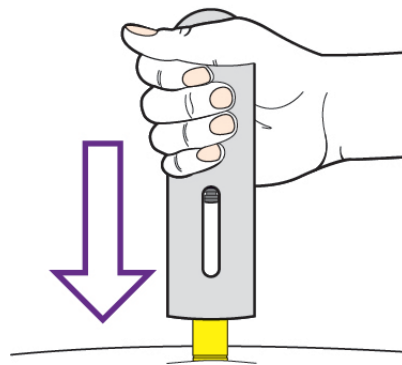
5. Inject Benlysta S.C. 200 mg

Start the injection

- Firmly press the pen all the way down onto the injection site and hold in place (*Figure 8*).

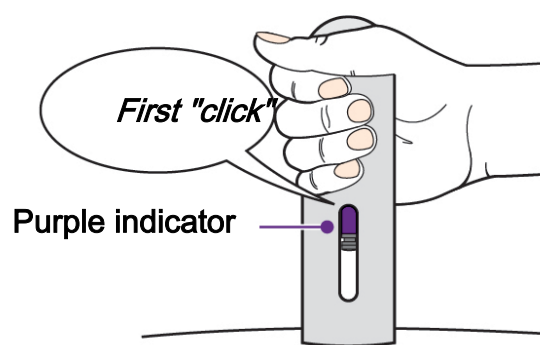
This will insert the needle and start the injection.

Figure 8



You may hear a first “click” at the start of the injection. You will notice that the purple indicator starts to move through the inspection window (*Figure 9*).

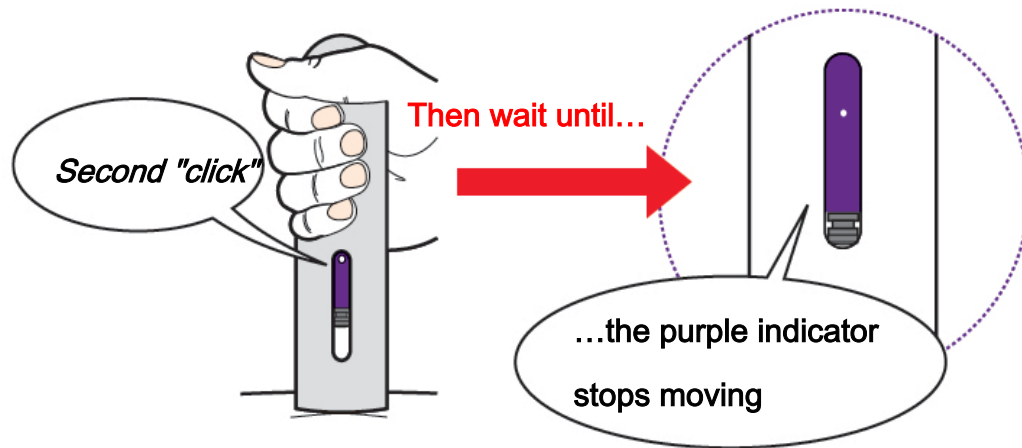
Figure 9



Complete the injection

Continue to hold the pen down until the purple indicator has stopped moving. You may hear a second “click” a few seconds before the purple indicator stops moving (*Figure 10*).

Figure 10



The injection may take up to 15 seconds to complete.

- When the injection is complete, lift the pen from the injection site.

6. Dispose and inspect

Dispose the used pen

- Do not put the ring cap back onto the pen.
- Dispose of the used pen and ring cap in an empty container with a tight-fitting lid.
- Ask your physician or pharmacist for instructions on how to properly dispose of a used pen or a container of used pens.
- **Do not** recycle or throw away the used pen, or container of used pens, into the household waste.

Inspect the injection site

There may be a small amount of blood at the injection site.

- If needed, press a cotton ball or gauze pad on the injection site.
- **Do not** rub the injection site.

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