Patient leaflet in accordance with the
Pharmacists' Regulations (Preparations) - 1986
This medicine is dispensed with a doctor's prescription only

Orencia 125 mg S.C.

Solution for subcutaneous injection

The active ingredient and its concentration:
Each ml of solution contains: abatacept 125 mg

For a list of inactive ingredients please see section 6 and "Important information about some of this medicine's ingredients" in section 2.
Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your doctor or pharmacist.
This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them, even if it seems to you that their illness is similar to yours.

1. What is this medicine intended for?

Orencia 125 mg Subcutaneous:

- Is intended to reduce signs and symptoms, induce major clinical response, inhibit the progression of structural damage, and improve physical functioning of adult patients with moderate to severe active rheumatoid arthritis. Orencia 125 mg Subcutaneous may be used in adults as monotherapy or concomitantly with disease-modifying antirheumatic drugs (DMARDs), other than tumor necrosis factor (TNF) antagonists.

- Orencia 125 mg Subcutaneous is intended to treat adult patients with active psoriatic arthritis (PsA).

Therapeutic group: Selective immunosuppressant

2. Before using this medicine:

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient abatacept or to any of the other ingredients in this medicine. See section 6 'Additional information' for a list of the other ingredients.

Special warnings about using this medicine:

- **Before you use Orencia 125 mg Subcutaneous, tell your doctor about all of your medical conditions, including if you:**
  - have any kind of infection even if it is small (such as an open cut or sore), or an infection that is in your whole body (such as the flu). If you have an infection

when taking Orencia 125 mg Subcutaneous, you have a higher chance of getting serious side effects.
- have an infection that will not go away or an infection that keeps coming back.
- have or have had inflammation of your liver due to an infection (viral hepatitis). Before you start to use Orencia 125 mg Subcutaneous, your doctor may examine you for hepatitis.
- have had a lung infection called tuberculosis (TB), received a positive skin test for TB, or you recently have been in close contact with someone who has had TB.
  Before you start to use Orencia 125 mg Subcutaneous, your doctor may examine you for TB or perform a skin test.
  Symptoms of TB may include: a cough that does not go away, weight loss, fever, and night sweats.
- are scheduled to have surgery.
- recently received a vaccination or are scheduled for a vaccination. While you are receiving Orencia 125 mg Subcutaneous, and for 3 months after you stop receiving Orencia 125 mg Subcutaneous, you must not receive live vaccines.
- have a history of a breathing problem called chronic obstructive pulmonary disease (COPD).
- Orencia 125 mg for subcutaneous injection (injected under the skin) does not contain maltose. You do not need to change your blood sugar monitoring if you are taking Orencia 125 mg Subcutaneous.
- are pregnant or plan to become pregnant, see the section 'Pregnancy and breastfeeding'.
- are breastfeeding or plan to breastfeed. See the section 'Pregnancy and breastfeeding'.
- Some people treated with Orencia have developed skin cancer. Tell your doctor if you have a family or personal history of skin cancer, and if you see any growths or changes in the appearance of your skin during or after your treatment with Orencia.
- you may have a higher chance of getting a serious infection if you use Orencia 125 mg Subcutaneous together with other biologic medicines for rheumatoid arthritis (RA) or psoriatic arthritis (PsA).

Children and adolescents:
Orencia 125 mg Subcutaneous is not intended for use in children and adolescents under 18 years old.

Drug interactions
If you are taking or have recently taken other medicines, including nonprescription medications and dietary supplements, tell your doctor or pharmacist.

Orencia 125 mg Subcutaneous may affect the way other medicines work, and other medicines may affect the way Orencia 125 mg Subcutaneous works, causing serious side effects. Especially if you are taking other biologic medicines to treat rheumatoid arthritis (RA) or psoriatic arthritis (PsA) that may affect your immune system, such as:
- etanercept
- adalimumab
- infliximab
- anakinra

- rituximab
- golimumab
- certolizumab pegol
- tocilizumab.

Pregnancy and breastfeeding:

Tell your doctor if you are pregnant or if you are planning a pregnancy. It is not known if Orencia 125 mg Subcutaneous can harm your unborn baby.
If you took Orencia 125 mg Subcutaneous during pregnancy, talk to your doctor before your baby receives any vaccines.
Tell your doctor if you are breastfeeding or plan to breastfeed. It is not known if Orencia 125 mg Subcutaneous passes into breast milk. Talk to your doctor about the best way to feed your baby if you are being treated with Orencia 125 mg Subcutaneous.

Important information about some of this medicine's ingredients:

Orencia 125 mg Subcutaneous contains less than 1 millimole (23 mg) of sodium per dose, so it is considered 'sodium free'.

3. How to use this medicine?

If your doctor decides that you or your caregiver can give your injections of Orencia 125 mg Subcutaneous in a prefilled syringe for use at home, you or your caregiver must receive training on the right way to prepare and inject Orencia 125 mg Subcutaneous. Do not try to inject Orencia 125 mg Subcutaneous until you have been instructed regarding the right way to give the injections by your healthcare provider (doctor or nurse).

For treatment of adults with Rheumatoid Arthritis

- The recommended dose of Orencia 125 mg Subcutaneous for treatment of adults with rheumatoid arthritis is usually a subcutaneous injection once a week.
  In some cases, at the initiation of treatment your doctor may give you a one-time infusion of a loading dose of Orencia IV. In this case, your subcutaneous injection of Orencia must be given within one day of the intravenous infusion.
- Patients switching from intravenous administration (infusion) to subcutaneous administration of Orencia – should receive the first subcutaneous injection instead of the next scheduled intravenous infusion.

For treatment of adults with Active Psoriatic Arthritis

- The recommended dose of Orencia 125 mg Subcutaneous for treatment of adults with psoriatic arthritis is usually a subcutaneous injection once a week.
- Patients on intravenous administration (infusion) of Orencia who switch to subcutaneous Orencia must receive their first subcutaneous injection instead of the nearest scheduled intravenous infusion.

- Always use this medicine according to the doctor's instructions.
- **See the instructions for preparing and giving your Orencia 125 mg Subcutaneous injection at the end of this patient information leaflet.**

Check with your doctor or pharmacist if you are not sure about the dosage and the treatment regimen of this medicine. The dosage and treatment regimen will be determined by the doctor only.

Do not exceed the recommended dose.

If you have injected a higher dose of the medicine, immediately see a doctor or go to a hospital emergency room and bring the medicine package with you.

Adhere to the treatment as recommended by your doctor.
Even if your health improves, do not stop taking this medicine without consulting your doctor or pharmacist.

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

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. Side effects:

Like with all medicines, using Orencia 125 mg Subcutaneous may cause side effects in some users. Do not be alarmed by this list of side effects. You may not experience any of them.

Orencia 125 mg Subcutaneous may cause serious side effects, including:

- **Infections.** Orencia 125 mg Subcutaneous may make you more likely to get infections or make the infection that you have get worse. Some people have died from these infections. Contact your doctor right away if you have any symptoms of an infection. Symptoms of an infection may include:
    - fever
    - feeling very tired
    - cough
    - flu-like symptoms
    - warm, red, or painful skin.

  The most common side effects resulting in clinical intervention (changes in treatment or discontinuation of ORENCIA treatment) in medicine administration were due to infection.

  The most commonly reported infections resulting in changes in the medicine dose were: upper respiratory tract infection, bronchitis, and herpes zoster.

  The most common infections resulting in discontinuation of treatment with the medicine were: pneumonia, localized infections, and bronchitis.

  The most commonly reported infections were: upper respiratory tract infection, inflammation of the throat and nose (nasopharyngitis), sinusitis, urinary tract infection, flu and bronchitis.

  Other infections reported were rhinitis, herpes simplex, and pneumonia.

  The most common serious infections reported were pneumonia, soft tissue infection (cellulitis), urinary tract infection, bronchitis, diverticulitis, and acute pyelonephritis.

- **Allergic reactions.** Allergic reactions can happen to people who use Orencia 125 mg Subcutaneous. Contact your doctor or go to the emergency room right away if you have any symptoms of an allergic reaction. Symptoms of an allergic reaction may include:
    - allergic rash (hives)
    - swollen face, eyelids, lips, or tongue
    - trouble breathing
    - hypotension.
- **Hepatitis B infection in people who carry the virus in their blood.** If you are a carrier of the hepatitis B virus (a virus that affects the liver), the virus can become active while you use Orencia 125 mg Subcutaneous. Your doctor may do blood tests before you start treatment with Orencia 125 mg Subcutaneous.
- **Vaccinations.** You should not receive Orencia 125 mg Subcutaneous with certain types of vaccines (live vaccines). You can receive non-live vaccines, such as pneumococcal and inactivated influenza (flu) vaccines. Orencia 125 mg Subcutaneous may also cause some vaccinations to be less effective.
  Talk to your doctor about your vaccination plans.
- **Breathing problems in people with Chronic Obstructive Pulmonary Disease - COPD.** You may get certain respiratory problems more often if you receive Orencia 125 mg Subcutaneous and have COPD. Symptoms of problems in the respiratory system, include:
    - COPD that becomes worse
    - cough
    - rhonchi
    - trouble breathing
    - pneumonia.

- **Cancer (malignancies).** Certain kinds of cancer have been reported in patients using Orencia 125 mg Subcutaneous. It is not known if Orencia 125 mg Subcutaneous increases your chance of getting certain kinds of cancer. The types of cancer that have been observed include lung cancer, lymphomas, skin cancer, breast cancer, bile duct cancer, bladder cancer, cervical cancer, endometrial cancer, melanoma, myelodysplastic syndrome, ovarian cancer, prostate cancer, kidney cancer, thyroid cancer, and uterine cancer.

Most common side effects of Orencia 125 mg Subcutaneous include:

- headache
- upper respiratory tract infection
- nausea
- inflammation of the throat and nose (nasopharyngitis).

Additional side effects:

- headaches
- inflammation of the throat and nose (nasopharyngitis)
- dizziness
- cough
- back pain
- hypertension
- digestion problems (dyspepsia)
- urinary tract infection
- rash

- pain in the extremities.

Injection site reactions in adult rheumatoid arthritis patients treated with Orencia 125 mg Subcutaneous included hematoma, pruritus, and erythema

Side effects reported after the medicine was placed on the market (postmarketing experience)

- inflammation of the blood vessels (vasculitis)
- new or worsening psoriasis
- non-melanoma skin cancers (basal cell carcinoma and squamous cell carcinoma)
- systemic injection reactions (e.g., pruritus, throat tightness, dyspnea)

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

Side effects can be reported to the Ministry of Health by clicking on the link: "Reporting of side effects from drug treatment", which can be found on the Ministry of Health homepage (www.health.gov.il) that 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?

- **Prevent poisoning!** To prevent poisoning, keep this, and all other medicines, in a closed place, out of the reach and sight of children and/or infants. Do not induce vomiting unless explicitly instructed to do so by a doctor.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.

Storage conditions:

- Store in the refrigerator between 2°C-8°C.
- Do not freeze the medicine. Store in the original package to protect from light.

Discard expired or out-of-use medicines safely.

6. Additional information:

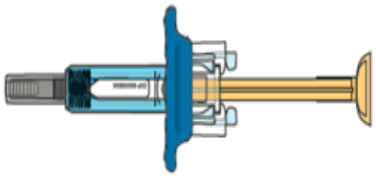
- **In addition to the active ingredient, this medicine also contains:**
  sucrose, poloxamer 188, disodium phosphate anhydrous, sodium phosphate monobasic monohydrate, water for injection.

- **What the medicine looks like and contents of the pack:**
  Each syringe contains 1.007 ml of a clear to slightly opalescent, colorless to pale yellow solution.
  A pack contains 1, 4, or 12 syringes. Not all pack sizes may be marketed.
- **Registration holder's name and address:** Bristol-Myers Squibb (Israel) Ltd., 18 Aharon Bart St., POB 3361, Kiryat Aryeh, Petah Tikva 4951448.
- **Manufacturer's name and address:**
  Bristol-Myers Squibb Holdings Pharma Ltd., Liability Company, Manati, Puerto Rico 00674, USA.

Revised in February 2021 according to MOH guidelines.

Registration number of the medicine in the Ministry of Health's National Drug Registry: 149-54-33788-00.

Instructions for preparing and giving your Orencia 125 mg Subcutaneous injection:



Orencia pre-filled syringe with BD UltraSafe Passive™ needle guard

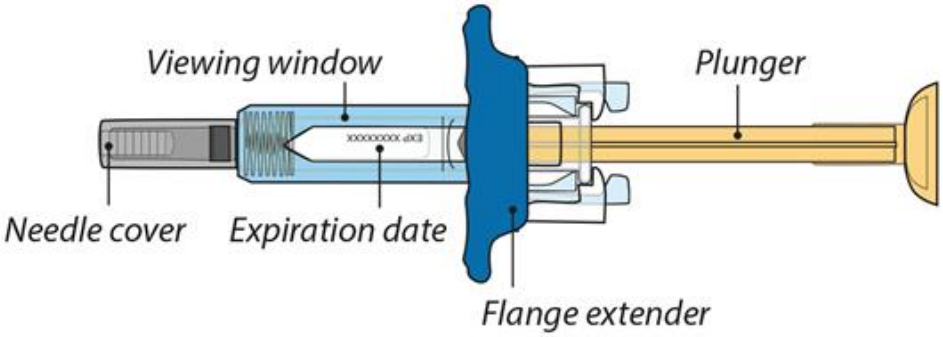
Read these instructions carefully before you use Orencia 125 mg Subcutaneous prefilled syringe for the first time and each time you use it. There may be new information in the instructions. Before you use the prefilled syringe for the first time, make sure your healthcare provider (doctor or nurse) instructed you regarding the right way to inject and decides that you or your caregiver are able to give your injections of Orencia 125 mg Subcutaneous at home.

Important:

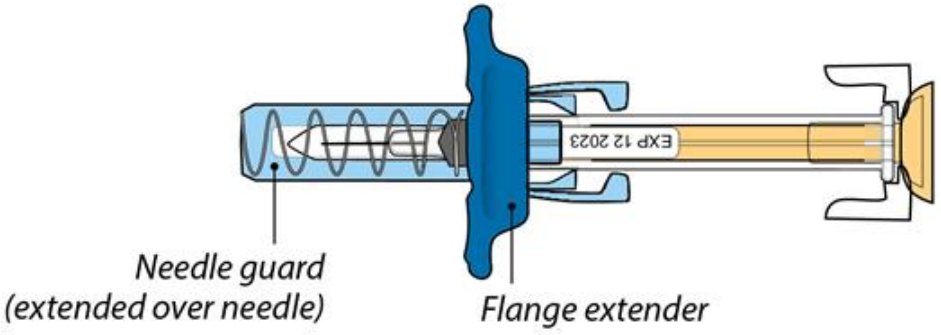
- **Keep the prefilled syringe in the refrigerator until you are ready to inject**
- **Do not freeze the syringe**

Before you begin: get to know your prefilled syringe

Before Use:



After use:



The prefilled syringe has a **handle (flange extender)** that makes it easier to hold while injecting, and a **needle guard** that automatically covers the needle after a complete injection**.**

DO NOT remove the needle cover until you are ready to inject.
DO NOT PULL back on the plunger at any time.
DO NOT RECAP the prefilled syringe at any time, as this may damage, bend, or break the needle.

Go to Step 1
Step 1: Preparing for Orencia 125 mg Subcutaneous injection

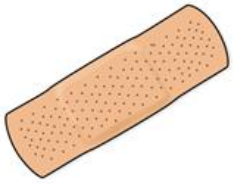
Gather and place all supplies for your injection on a clean, flat surface.

Only the prefilled syringe is included in the package.

- Alcohol swab

- Prefilled Syringe with UltraSafe Passive Needle Guard

- Adhesive bandage



- Sharps disposal container

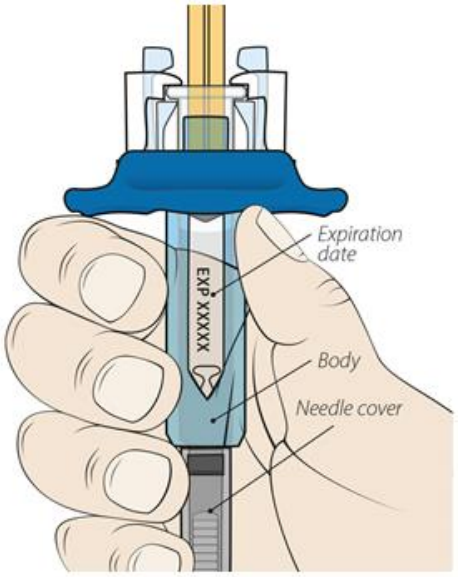
- Cotton ball or gauze

	**Let your prefilled syringe warm up.** Remove one prefilled syringe from the refrigerator and wait **30 minutes** to allow it to reach room temperature. ○ **Do not** speed up the warming process in any other way, such as using the microwave or placing the syringe in warm water. ○ **Do not** remove the needle cover while allowing the prefilled syringe to reach room temperature.

Wash your hands well with soap and water.

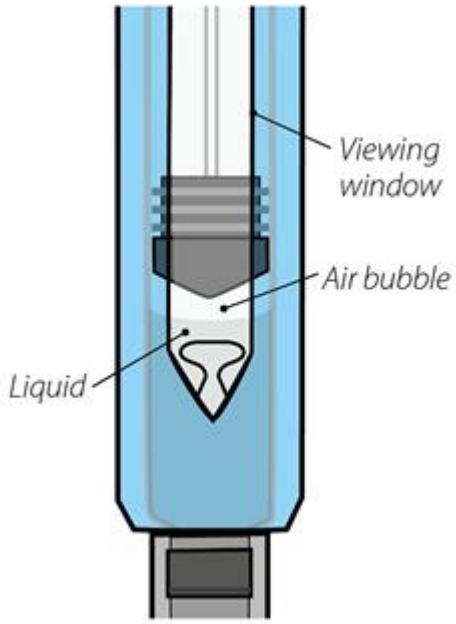
Go to Step 2.

Step 2: Examine the Prefilled Syringe



Hold the prefilled syringe by the body with the needle cover pointing down. (see figure).

- **Check the expiration date** printed on the label. **Do not** use the medicine if the expiration date has passed.
- **Check the prefilled syringe for damage.**
  Do not use if it is cracked or broken.



Check the Liquid.

- **Check the liquid** in the prefilled syringe through the viewing window. It should be clear, and colorless to pale yellow.

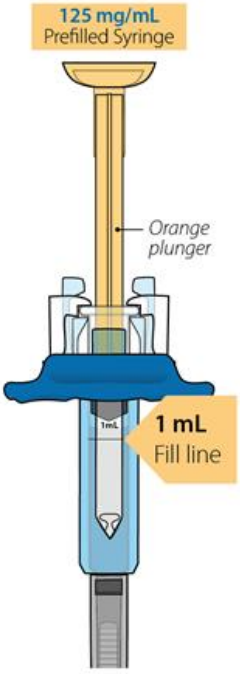
Do not inject if the liquid is **cloudy, discolored, or has particles in it.**

Note: It is normal to see an air bubble. Do not attempt to remove it.

Go to Step 3.

Step 3: Check the dose on the prefilled syringe

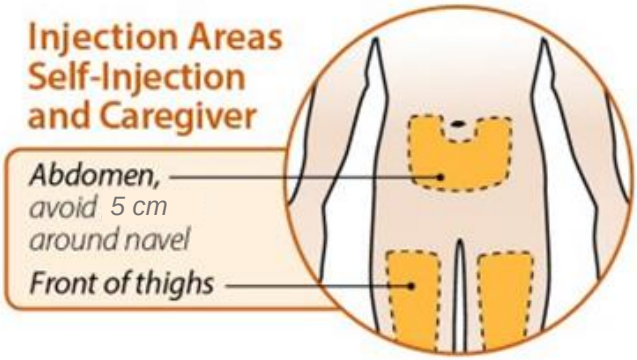
Hold the syringe at eye level. Look closely to make sure that the amount of liquid in the prefilled syringe **is at or just above the fill line:**



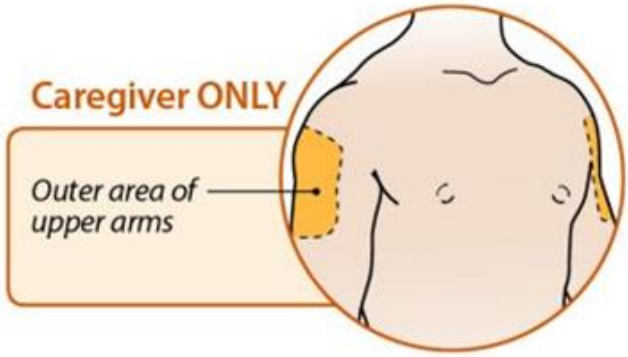
Do not use if your prefilled syringe does not have the correct amount of liquid. Call your pharmacist immediately.

Go to Step 4.

Step 4: Choose and prepare your injection site



Choose your injection site.
Choose your injection site in either the stomach **(abdomen)**, or front of the **thighs** or outer area of **upper arm** (only if caregiver administered).

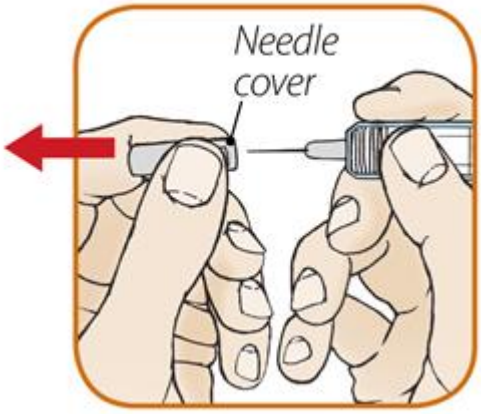


Rotate the injection site each time:

- Each week you can use the same area of your body, but use a different injection site in that area.
- **Do not** inject into an area where the skin is tender, bruised, red, scaly, or hard. **Avoid** giving the injection in any areas with scars or stretch marks.
- Record the date, time, and site where you injected.

Gently clean the injection site.

- Wipe the injection site with an alcohol swab and let it air dry.
- **Do not** touch the injection site again before giving the injection.
- **Do not** blow on the clean injection area.



Remove the needle cover by holding the body of the prefilled syringe with one hand and pulling the cover off with your other hand.

Do not put the needle cover back on the needle after you remove it. Throw away the needle cover in your household trash.

- **Do not** use the prefilled syringe if it is dropped after the needle cover is removed.
- **Do not** use the prefilled syringe if the needle is damaged or bent.

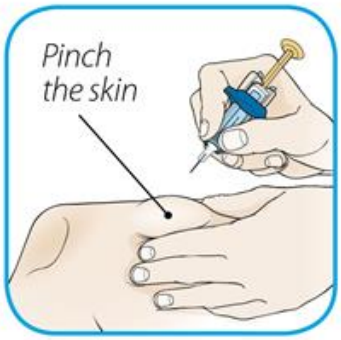
Note: It is normal to see a drop of fluid leaving the needle.

DO NOT RECAP the needle of the prefilled syringe, as this may damage the needle.

Go to Step 5

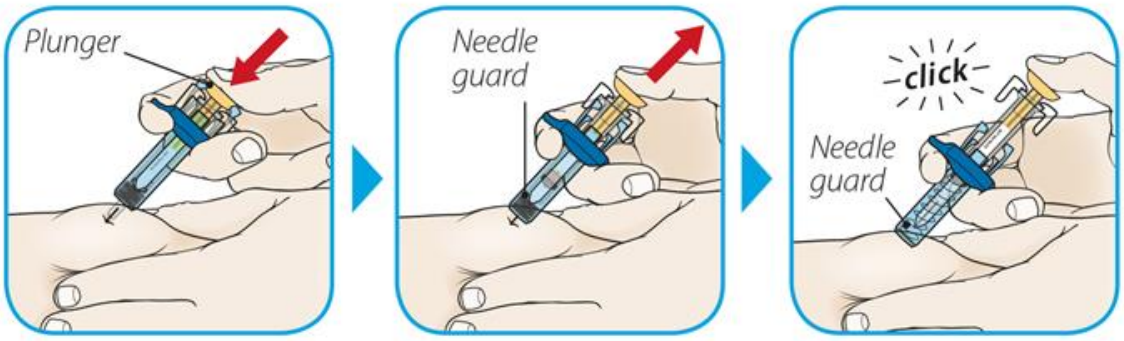
Step 5: Inject your dose of Orencia 125 mg Subcutaneous

Hold the body of the prefilled syringe in your hand using your thumb and index finger. With your free hand, **pinch the area of skin you cleaned.**



Insert the needle.
Gently insert the needle into the pinched skin at a 45° angle.

Complete all the steps in order to get a full dose of the medicine.



Inject: **Push the plunger** with your thumb as far as it will go.	**Release Needle Guard: Slowly lift your thumb from the plunger** to activate the needle guard.	**Confirm:** After a complete injection, **the needle guard will cover the needle** and you may hear a click.

Remove the prefilled syringe and let go of the pinched skin.

Go to Step 6

Step 6: After the injection
Care of injection site:

- There may be a little bleeding at the injection site.
  You can press a cotton ball or gauze over the injection site.
- **Do not** rub the injection site.
- If needed, you may cover the injection site with an adhesive bandage.

Disposing of used syringes:

- Put your used Orencia 125 mg Subcutaneous syringe in a sharps disposal container right away after use.
  Do not throw away used needles and syringes in your household trash.
- If you do not have a sharps disposal container, you may use a household trash container that is:
  - made of a heavy-duty plastic
  - can be closed with a tight-fitting, puncture-resistant lid, so that syringes can't fall out of the container
  - upright and stable during use
  - leak resistant
  - properly labeled to warn of hazardous waste inside the container

Do not throw away your sharps disposal container in your household trash. **Do not** recycle your used sharps disposal container.

If the injection is administered to you by another person, this person must be careful while handling the syringe to prevent accidental needle stick injury and possible spreading of infection.

Keep Orencia 125 mg Subcutaneous prefilled syringes, and the sharps disposal container out of the reach of children.