PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986
The medicine is dispensed with a doctor's prescription only

Ustekinumab Kamada Pre-filled Syringe, 45 mg solution for injection Ustekinumab Kamada Pre-filled Syringe, 90 mg solution for injection

Active ingredient and its quantity:
Ustekinumab 90 mg/mL
- Each 0.5 ml pre-filled syringe contains ustekinumab 45 mg
- Each 1 ml pre-filled syringe contains ustekinumab 90 mg

Inactive and allergic ingredients in the preparation – see section 6 "further information".
Read the leaflet carefully in its entirety before you start using the medicine. This leaflet contains concise information about the medicine. If you have any further questions, refer to the doctor 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.
Ustekinumab Kamada Pre-filled Syringe is a biosimilar product. For more information regarding biosimilar products, please refer to the Ministry of Health website:
https://www.gov.il/he/Departments/General/biosimilar

1. WHAT IS THE MEDICINE INTENDED FOR?

Plaque psoriasis
Ustekinumab Kamada is indicated for the treatment of moderate to severe plaque psoriasis in adult patients (18 years or older) who have failed to, have a contraindication to, or who are intolerant to other systemic therapies including ciclosporin, methotrexate (MTX) or psoralen plus UV (PUVA).

Paediatric plaque psoriasis
Ustekinumab Kamada is indicated for the treatment of moderate to severe plaque psoriasis in children and adolescent patients from the age of 6 years and older (weighing at least 60 kg), who are inadequately controlled by, or are intolerant to, other systemic therapies or phototherapies.

Psoriatic arthritis (PsA)
Ustekinumab Kamada, alone or in combination with MTX, is indicated for the treatment of active psoriatic arthritis in adult patients when the response to previous non-biological disease-modifying anti-rheumatic drug (DMARD) therapy has been inadequate.

Crohn's Disease
Ustekinumab Kamada is indicated for the treatment of adult patients with moderately to severely active Crohn's disease who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a TNFα antagonist or have medical contraindications to such therapies.

Ulcerative colitis
Ustekinumab Kamada is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic or have medical contraindications to such therapies.

Therapeutic group: interleukin inhibitors
Ustekinumab Kamada contains the active substance ustekinumab, which is a monoclonal antibody. Monoclonal antibodies are proteins that recognize and bind specifically to certain proteins in the body. Ustekinumab Kamada belongs to a group of medicines called "immunosuppressants". These medicines work by weakening part of the immune system.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:
- You are sensitive (allergic) to the active ingredient or any of the additional ingredients of this medicine listed in section 6 "Further information".
- You are suffering from an active infection which your doctor thinks is important.

If you are unsure if the above applies to you, consult the doctor or pharmacist before you start using Ustekinumab Kamada.

Special warnings regarding use of the medicine
Talk to the doctor before you start using Ustekinumab Kamada. The doctor will check your condition before each treatment. Tell the doctor about any illness you have before each treatment. Also tell the doctor if you have recently been near anyone who might have tuberculosis. The doctor will examine you and do a test for tuberculosis before starting Ustekinumab Kamada treatment. If the doctor thinks you are at risk of tuberculosis, he may give you medicinal treatment.

Look out for serious side effects
Ustekinumab Kamada can cause serious side effects, including allergic reactions and infections. Look out for certain signs of illness during the course of treatment with Ustekinumab Kamada. See "Serious side effects" in section 4 "Side effects" for a full list of these signs.

Before treatment with Ustekinumab Kamada tell the doctor:
- **If you ever had an allergic reaction to ustekinumab**. If you are not sure, ask the doctor.
- **If you have ever had any type of cancer** – this is because immunosuppressants like ustekinumab weaken part of the immune system. This may increase the risk of cancer.
- **If you have been treated in the past with other biologic medicines (a medicine produced from a biological source and usually given by injection) for psoriasis**, the risk of cancer may be higher.
- **If you have or have recently had an infection**.
- **If you have any changes in lesions or new lesions** within psoriasis areas or on normal skin.
- **If you are receiving any other treatment for psoriasis and/or psoriatic arthritis**, such as another immunosuppressant or phototherapy (treatment with a type of UV light). These treatments may also weaken part of the immune system. These treatments in combination with ustekinumab have not been studied. However, such treatment may increase the risk of diseases related to a weaker immune system.
- **If you are receiving or have ever received injections to treat allergies** – it is not known if ustekinumab may affect these.
- **If you are 65 years of age or over** – you may be more likely to get infections. If you are not sure if any of the above conditions apply to you, consult the doctor before using Ustekinumab Kamada.

Some patients have experienced lupus-like reactions including skin lupus or lupus-like conditions during treatment with ustekinumab. Talk to the doctor right away if you experience a red, raised, scaly rash sometimes with a darker border, in areas of the skin that are exposed to the sun or with joint pains.

Heart attack and strokes
Heart attacks and strokes have been observed in a study in patients with psoriasis treated with ustekinumab. Your doctor will regularly check your risk factors for heart disease and stroke to ensure that they are being treated properly. Seek medical assistance immediately if you develop chest pain, weakness or an abnormal sensation on one side of your body, facial droop, or speech or vision disturbances.

Children and adolescents
Ustekinumab Kamada is not intended for treatment of psoriasis in children under 6 years of age, and for psoriatic arthritis, Crohn's disease or ulcerative colitis in children and adolescents under 18 years of age, since it was not tested in this age group.
Ustekinumab Kamada Pre-filled Syringe is not suitable for treating psoriasis in paediatric patients below 60 kg of body weight, and other ustekinumab products allowing weight-based dosing must be used.

Drug interactions
If you are taking, or have recently taken, other medicines, including non-prescription medicines, nutritional supplements, and vaccines, tell the doctor or pharmacist. In particular:
- If you have recently received a vaccination or are due to receive a vaccination. Do not receive certain vaccinations (that contain a live vaccine) during the course of treatment with Ustekinumab Kamada.
- If you received Ustekinumab Kamada while pregnant, tell your baby's doctor about your Ustekinumab Kamada treatment before the baby receives any vaccine, including live vaccines, such as the BCG vaccine (used to prevent tuberculosis). Live vaccines are not recommended for your baby in the first six months after birth if you received Ustekinumab Kamada during the pregnancy unless your baby's doctor recommends otherwise.

Pregnancy and breast-feeding
- It is preferable to avoid the use of Ustekinumab Kamada in pregnancy. The effect of ustekinumab on pregnant women is not known. If you are a woman of childbearing potential, avoid becoming pregnant by using adequate contraception during treatment with Ustekinumab Kamada, and for at least 15 weeks after the last Ustekinumab Kamada treatment.
- Tell the doctor if you are pregnant, think you may be pregnant, or are planning to become pregnant.
- Ustekinumab can pass across the placenta to the unborn baby. If you received ustekinumab during pregnancy, your baby may have a higher risk for getting infections.
- It is important that you tell your baby's doctors and other health care professionals if you received ustekinumab during pregnancy before the baby receives any vaccine. Live vaccines such as the BCG vaccine (used to prevent tuberculosis) are not recommended for your baby in the first six months after birth if you received ustekinumab during the pregnancy unless your baby's doctor recommends otherwise.
- Ustekinumab may pass into breast milk in very small amounts. Tell the doctor if you are breast-feeding or are planning to breast-feed. You and the doctor should decide if you should breast-feed or use Ustekinumab Kamada. Do not do both.

Driving and using machines
Ustekinumab Kamada has no or negligible influence on the ability to drive and use machines.

3. HOW SHOULD THE MEDICINE BE USED?

Ustekinumab Kamada is intended for use under the instructions and supervision of a doctor experienced in treating conditions for which Ustekinumab Kamada is intended.
Always use the medicine in accordance with the doctor's instructions.
Check with the doctor or pharmacist if you are not sure regarding the medicine dosage and treatment regimen. Talk to the doctor about the injection administration schedule and follow-up appointments.
The dosage, frequency, duration of treatment and treatment method will be determined by the doctor only.

The usual dosage is generally:
Adults aged 18 years or older:
Psoriasis or psoriatic arthritis
- The recommended initial dose is 45 mg Ustekinumab Kamada Pre-filled Syringe. Patients who weigh more than 100 kilograms (kg) may start on a dose of 90 mg instead of 45 mg.
- After the initial dose, you will have the second dose 4 weeks later, and then every 12 weeks. The following doses are usually the same as the starting dose.

Crohn's disease or Ulcerative colitis
- **Ustekinumab Kamada is only available in pre-filled syringes for subcutaneous use. Since treatment of Crohn's disease and ulcerative colitis should be initiated by intravenous infusion, another ustekinumab product must be used as first intravenous dose (130 mg concentrate for solution for infusion).**
- Ustekinumab Kamada is administered by injection under the skin (subcutaneously). You will receive the first dose of 90 mg Ustekinumab Kamada 8 weeks after the intravenous infusion, then every 12 weeks thereafter subcutaneously.
- In some patients, after the first injection under the skin, 90 mg Ustekinumab Kamada may be given every 8 weeks. The doctor will decide when you should receive your next dose.

Children and adolescents aged 6 years or older
Psoriasis
- The doctor will calculate the right dose for you, including the amount (volume) of Ustekinumab Kamada to be injected that contains this dose. The right dose for you will depend on your body weight at the time it is given.
- If you weigh less than 60 kg, there is no available dosage form of Ustekinumab Kamada for children below 60 kg body weight. Ustekinumab Kamada is only available as 45 mg and 90 mg solution for injection in pre-filled syringe. Thus, it is not possible to administer Ustekinumab Kamada to patients that require less than a full 45 mg dose. If an alternate dose is required, another ustekinumab product 45 mg solution for injection in vials offering weight-based dosing should be used instead.
- If you weigh between 60 kg to 100 kg, the recommended dose is 45 mg Ustekinumab Kamada.
- If you weigh more than 100 kg, the recommended dose is 90 mg Ustekinumab Kamada.
- After the first dose, you will have the second dose 4 weeks later, and then every 12 weeks.

Do not exceed the recommended dose.

How Ustekinumab Kamada is given:
- Ustekinumab Kamada is given as an injection under the skin (subcutaneously). At the beginning of treatment, a nurse or healthcare professional may inject the medicine.
- However, if you decide with your doctor that you can inject the medicine yourself, you will have to undergo training on how to do this.
- For instructions on how to inject Ustekinumab Kamada, see 'Instructions for use' at the end of this leaflet.

Consult a doctor if you have questions about self-injecting the medicine.

If you have accidentally taken a higher dosage:
Contact the doctor or pharmacist immediately. Bring the outer package of the medicine with you, even if it is empty.

If you forget to use the medicine:
Contact the doctor or pharmacist if you have forgotten to inject a dose of Ustekinumab Kamada. Do not inject two doses to compensate for a forgotten dose. Adhere to the treatment as recommended by the doctor.

If you stop using the medicine:
It is not dangerous to stop the Ustekinumab Kamada treatment. However, stopping treatment may lead to a recurrence of the signs of the disease. Consult the doctor if you are interested in discontinuing treatment.

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

If you have any further questions regarding the use of the medicine, consult a doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Ustekinumab Kamada may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Serious side effects - Some patients may suffer from serious side effects that may need urgent treatment.

(X) An allergic reaction – may need urgent treatment. Inform the doctor immediately or proceed to an emergency room to receive urgent medical treatment if you notice any of the following signs:
Severe allergic reaction ('anaphylaxis') is rare in patients treated with ustekinumab (may occur in up to 1 in 1,000 users). Signs include:
- Difficulty in breathing or swallowing.
- Low blood pressure, which may cause dizziness or light-headedness.
- Swelling of the face, lips, mouth, or throat.

Common signs of an allergic reaction include skin rash and hives (which can occur in up to 1 in 100 users).

In rare cases, a pulmonary allergic reactions and lung inflammation have been reported in patients being treated with ustekinumab. Tell the doctor immediately if symptoms such as cough, shortness of breath, and fever start to develop.

If you experience a severe allergic reaction, the doctor may decide that you should not use Ustekinumab Kamada again.

(X) Infections – these may require urgent treatment. Inform the doctor immediately if you notice any of the following signs:
- Infections of the nose or throat and common cold occur frequently (common) (can occur in up to 1 in 10 users).
- Infections of the chest are uncommon (can occur in up to 1 in 100 users).
- Inflammation of tissue under the skin (cellulitis) is uncommon (can occur in up to 1 in 100 users).
- Shingles (a type of painful rash with blisters) are uncommon (can occur in up to 1 in 100 users).

Ustekinumab Kamada may weaken the body's ability to fight infections. Certain infections may worsen and may include infections caused by viruses, fungi, bacteria (including tuberculosis), or parasites, including infections that mainly occur in people with a weakened immune system (opportunistic infections). Opportunistic infections of the brain (encephalitis, meningitis), lungs, and eye have been reported in patients receiving treatment with ustekinumab.

While using Ustekinumab Kamada, monitor symptoms of infection. The symptoms include:
- fever, flu-like symptoms, night sweats, weight loss
- feeling tired or short of breath; persistent cough
- warm, red, and painful skin, or a painful skin rash with blisters
- a burning sensation when urinating
- diarrhoea
- visual disturbance or vision loss
- headache, neck stiffness, light sensitivity, nausea, or confusion.

Inform the doctor immediately if you notice any symptoms of infection. These can be symptoms of infections such as chest infections, skin infections, shingles, or opportunistic infections that could have serious complications. Inform the doctor if you have an infection that does not go away or keeps coming back. The doctor may decide that you should not use Ustekinumab Kamada until the infection goes away. In addition, tell the doctor if you have open cuts or sores on your skin, since they may become infected.

(X) Shedding of skin – an increase in redness and shedding of skin over a larger areas of the body may be symptoms of erythrodermic psoriasis or exfoliative dermatitis, which are serious skin conditions. Inform the doctor immediately if you notice these signs.

Additional side effects:

Common side effects - effects that may occur in up to 1 in 10 users:
- Diarrhoea
- Nausea
- Vomiting
- Tiredness
- Dizziness
- Headache
- Itching
- Back pain, muscle or joint pain
- Sore throat
- Redness and pain in the injection site
- Sinus infection

Uncommon side effects - effects that may occur in up to 1 in 100 users:
- Tooth infections
- Vaginal yeast infection
- Depression
- Blocked or nasal congestion.
- Bleeding, bruising, hardening of the skin, swelling and itching/stinging at the injection site.
- Weakness
- Drooping eyelid and muscles weakness on one side of the face (facial paralysis or Bell's palsy)-this effect is usually temporary.
- A change in psoriasis with redness and new small, yellow, or white-colored blisters on the skin, sometimes accompanied by fever (pustular psoriasis).
- Skin exfoliation
- Acne

Rare side effects - effects that may occur in up to 1 in 1,000 users:
- Redness and shedding of skin over larger areas of the body, which may be itchy or painful (exfoliative dermatitis). Similar symptoms sometimes develop as a natural change in the type of psoriasis symptoms (erythrodermic psoriasis).
- Inflammation of small blood vessels, which can lead to a skin rash with small red or purple bumps, fever, or joint pain (vasculitis).

Very rare side effects - effects that may occur in up to 1 in 10,000 users:
- Blistering of the skin that may be red, itchy, and painful (Bullous pemphigoid).
- Skin lupus or lupus-like syndrome (red, raised scaly rash on areas of the skin exposed to the sun possibly with joint pains).

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

Reporting of 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.il) that directs you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il
Additionally, you may also report to Kamada Ltd. at the email address: pharmacovigilance@kamada.com

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine and any other medicine should be kept in a safe place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.

Do not use this medicine:
- After the expiry date (exp. Date) that appears on the package. The expiry date refers to the last day of that month.
- If the liquid is discolored, cloudy or you can see other foreign particles floating in it (see section 6 'Further information').
- If you know or think that the medicine may have been exposed to extreme temperatures (such as accidentally frozen or heated).
- If the product has been shaken vigorously.

Storage conditions:
- Store in a refrigerator (2°C–8°C). Do not freeze. For single use only.
- Keep the pre-filled syringe in the outer carton in order to protect from light.
- The pre-filled syringe should be allowed to reach room temperature (approximately half an hour).
- If needed, individual Ustekinumab Kamada pre-filled syringes may also be stored at room temperature up to 30°C for a maximum single period of up to 30 days in the original carton in order to protect from light. Record the date when the pre-filled syringe was first removed from the refrigerator in the designated space on the outer carton. The date of discard into a designated container must not be later than the expiry date printed on the carton. If a syringe has been stored at room temperature (up to 30°C), do not return it to the refrigerator. Discard the syringe into a designated container if not used within 30 days at room temperature storage or by the original expiry date, whichever is earlier.
- Do not shake the pre-filled syringes. Prolonged vigorous shaking may damage the medicine.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:
Sucrose, L-histidine monohydrochloride monohydrate, L-histidine, polysorbate 80, water for injection.

What the medicine look like and contents of the pack:
Clear, colorless to slightly yellow, and practically free of visible particles solution for injection.

Each box contains one pre-filled glass syringe.
Package sizes:
1 pre-filled syringe containing 45 mg/0.5 ml ustekinumab.
1 pre-filled syringe containing 90 mg/1 ml ustekinumab.

Marketing Authorization Holder
Kamada Ltd., Beit-Kama, MP Negev 8532500

Manufacturer
Alvotech Hf
Sæmundargata 15-19
Reykjavik, 102
Iceland

Revised in July 2024 according to MOHs guidelines.

The drug registration number in the National Drug Registry in the Ministry of Health:
176-94-37976-00

INSTRUCTION FOR USE
Ustekinumab Kamada Pre-filled Syrine, solution for subcutaneous injection

Read carefully these instructions for use before using Ustekinumab Kamada solution for injection in pre-filled syringe.

At the beginning of treatment, the healthcare provider will assist you with your first injection. However, if you decide with the doctor you can self-inject Ustekinumab Kamada, you will undergo training on how to inject the medicine yourself. Consult the doctor if you have any questions about self-injection.

Important information you need to know before injecting the solution of Ustekinumab Kamada Pre-filled Syringe:
Ustekinumab Kamada Pre-filled Syringe solution is not suitable for intravenous use. Other ustekinumab products must be used for the initiation of treatment of Crohn's disease and ulcerative colitis.
Ustekinumab Kamada Pre-filled Syringe solution is not suitable for paediatric patients below 60 kg of body weight, other ustekinumab products allowing weight-based dosing must be used.

Important information:
- For subcutaneous use only.
- Do not mix Ustekinumab Kamada with other liquids for injection.
- Do not shake the syringes. This is because shaking may damage the medicine. Do not use the medicine if it has been shaken. Get a new pre-filled syringe.

Ustekinumab Kamada Pre-filled Syringe does not contain preservatives, and therefore, do not use any unused solution remaining in the syringe after the injection. Ustekinumab Kamada Pre-filled Syringe is a sterile, single use product.

Check the pre-filled syringe(s) to make sure:
- the number of pre-filled syringes and strength is correct:
  - If you have to inject 45 mg, use one 45 mg Ustekinumab Kamada Pre-filled Syringe.
  - If you have to inject 90 mg, you may use one 90 mg Ustekinumab Kamada syringe or use two 45 mg syringes. In the second case, you will have to inject yourself with two injections. Choose 2 different areas of the body (e.g., one injection in the right thigh and the other in the left thigh) and inject one injection after the other.
- it is the right medicine.
- it has not passed its expiry date.
- the pre-filled syringe is not damaged.
- the solution in the pre-filled syringe is clear and colourless to slightly yellow and practically free of visible particles.
- the solution in the pre-filled syringe is not frozen.
- it should be allowed to reach room temperature (approximately half an hour).

Figure 1 shows what the Ustekinumab Kamada Pre-filled Syringe looks like.

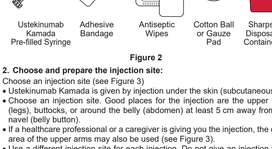

Figure 1

1. Prepare the materials
Gather the supplies you will need to prepare and to give your injection. You will need:
- Antiseptic wipes
- Cotton balls or gauze pads
- Adhesive bandage
- Your prescribed dose of Ustekinumab Kamada (see Figure 1).
- Puncture-resistant sharps disposal container (not included). See Figure 2.

Get everything together that you need and lay out on a clean surface.

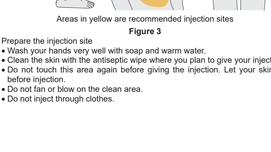

Figure 2

2. Choose and prepare the injection site:
Choose an injection site (see Figure 3)
- Ustekinumab Kamada is given by injection under the skin (subcutaneously).
- Choose an injection site. Good places for the injection are the upper thigh (legs), buttocks, or around the belly (abdomen) at least 5 cm away from the navel (belly button).
- If a healthcare professional or a caregiver is giving you the injection, the outer area of the upper arms may also be used (see Figure 3).
- Use a different injection site for each injection. Do not give an injection in an area of the skin that is tender, bruised, red or hard.

Areas in yellow are recommended injection sites

Figure 3

Prepare the injection site
- Wash your hands very well with soap and warm water.
- Clean the skin with the antiseptic wipe where you plan to give your injection.
- Do not touch this area again before giving the injection. Let your skin dry before injection.
- Do not fan or blow on the clean area.
- Do not inject through clothes.

3. Remove the needle cover (see Figure 4):
- Remove the needle cover when you are ready to inject Ustekinumab Kamada.
- Do not touch the plunger while removing the needle cover.
- Hold the body of the pre-filled syringe with one hand, and pull the needle cover straight off (see Figure 4).
- Put the needle cover in the trash. Do not recap.
- You may also see a drop of liquid at the end of the needle. This is normal.
- Do not touch the needle or let it touch anything.
- Inject the dose promptly after removing the needle cover.

Figure 4

4. Inject the dose:
Grasp the syringe:
- Hold the body of the pre-filled syringe with one hand between the thumb and index finger (see Figure 5).
- Do not use the pre-filled syringe if it is dropped without the needle cover in place. If this happens, please contact your doctor or pharmacist for instructions.
- Do not pull back on the plunger at any time.

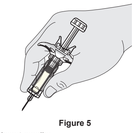

Figure 5

Pinch the skin and insert needle:
- Use the other hand to gently pinch the cleaned area of the skin. Hold firmly.
- Use a quick, dart-like motion to insert the needle into the pinched skin at about 45-degree angle (see Figure 6).

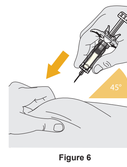

Figure 6

Inject the drug:
- Inject all of the liquid by using your thumb to push in the plunger all the way in until the prefilled syringe is empty (see Figure 7).

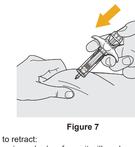

Figure 7

Allow the needle to retract:
- When the plunger is pushed as far as it will go, keep pressure on the plunger head. Take the needle out of the skin and let go of the skin.
- Slowly take your thumb off the plunger head. The plunger will move up with your finger and retract the needle into the needle guard (see Figure 8).

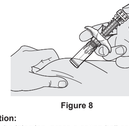

Figure 8

5. After the injection:
- After completing the injection, press a cotton ball or gauze pad on the skin of the injection site for a few seconds after the injection (see Figure 9).
- There may be a slight bleeding at the injection site. This is normal.
- Do not rub the skin at the injection site.
- You may cover the injection site with a small adhesive bandage, if necessary

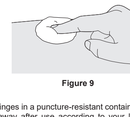

Figure 9

6. Disposal:
- Put the used syringes in a puncture-resistant container, like a sharps disposal container right away after use according to your local regulations. Do not throw away (dispose of) loose syringes in your household garbage (see Figure 10).
- Dispose of the antiseptic wipes, cotton ball or gauze pad, and packaging in your garbage.
- Never re-use a syringe, for your safety and health, and the safety of others.

Figure 10