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

The medicine is dispensed with a doctor's prescription only

ELIGARD 22.5 mg
powder and solvent for solution for injection

Active ingredient and its quantity:
Syringe B contains: Leuprorelin acetate **22.5** mg

Excipients and allergens in the product – see section 6 "additional information".

Read this 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 only. Do not pass it on to others. It may harm them, even if it seems to you that their ailment is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

ELIGARD is indicated for the treatment of hormone dependent advanced **prostate cancer** and for the treatment of high-risk localized and locally advanced hormone dependent prostate cancer in combination with radiotherapy.

Therapeutic group: analogs to gonadotropin releasing hormones.

These medicines are used to decrease the production of certain sex hormones (testosterone).

2. BEFORE USING THE MEDICINE

Do not use the medicine:

- If you are a **woman** or a **child**
- If you are **hypersensitive (allergic)** to the active substance leuprorelin acetate, products with an activity comparable to the naturally occurring hormone gonadotropin, or to any of the other ingredients of ELIGARD (listed in section 6).
- Following **surgical removal of your testes**, as in that case ELIGARD does not lead to a further decrease in serum testosterone levels.
- As the only treatment if you suffer from symptoms related to pressure on the spinal cord or tumour in the spinal column. In this case, ELIGARD may only be used in combination with other medicinal products for prostate cancer.

Special warnings regarding the use of the medicine

Talk to your doctor before using ELIGARD
- If you have any of the following: Any heart or blood vessel conditions, including heart rhythm problems (arrhythmia), or are being treated with medicines for these conditions. The risk of heart rhythm problems may be increased when using ELIGARD.
- If you have **difficulties urinating**. You should be monitored closely during the first weeks of treatment.
- If **pressure on the spinal cord or difficulties with urinating develops**. In connection with other drugs having a similar mechanism of action like ELIGARD, it has been reported that severe cases of pressure effects on the spinal cord and narrowing of the tubes between the

kidneys and the urinary bladder may contribute to paralysis like symptoms. If these complications develop, standard therapy should be started.
- If you experience sudden headache, vomiting, altered mental status and sometimes heart collapse, within two weeks of taking ELIGARD, then alert the doctor or medical staff. These are rare cases termed as pituitary apoplexy, which have been reported IN OTHER DRUGS which have a mechanism similar to ELIGARD.
- If you suffer from **diabetes mellitus** (elevated blood sugar levels). You should be regularly monitored during treatment.
- Treatment with ELIGARD can increase the risk for fractures due to osteoporosis (decrease in bone density).
- There have been reports of depression in patients taking ELIGARD. If you are taking ELIGARD and develop depressed mood, inform your doctor.
- There have been reports of cardiovascular events in patients taking products similar to ELIGARD of which it is unknown if it is related to these products. If you are taking ELIGARD and develop cardiovascular signs or symptoms, inform your doctor.
- There have been reports of seizures in patients after administration of ELIGARD. If you are taking ELIGARD and develop seizures, inform your doctor.
- If you suffer from a bad or recurrent headache, problems with your eyesight and ringing or buzzing in the ears contact your doctor immediately.
- If you have fatty liver.

Severe skin rashes including Stevens-Johnson syndrome, Toxic Epidermal Necrolysis (SJS/TEN) have been reported in association with leuprorelin. Stop using leuprorelin and seek medical attention immediately if you notice any of the symptoms related to these serious skin reactions described in section 4.

Complications due to initial treatment with ELIGARD

During the first week of treatment, there is generally a brief increase in the male sex hormone testosterone in the blood. This can lead to **a temporary worsening** in the disease-related symptoms and also to the occurrence of new symptoms that have not been experienced up to this point. These especially include bone pain, urination disturbances, pressure on the spinal cord, or the secretion of blood in the urine. These symptoms usually subside on continuation of treatment. If the symptoms do not subside, you should contact your doctor.

If treatment with ELIGARD does not help

A proportion of the patients will have tumors, which are not sensitive to decreased serum testosterone levels. Please talk to your doctor if you have the impression that the effect of ELIGARD is too weak.

Use of other medicines and ELIGARD

If you are taking, or have recently taken other medicines, including non-prescription medicines and dietary supplements, tell this to your doctor or pharmacist. Especially if you are taking:

ELIGARD might interfere with some medicines used to treat heart rhythm problems (e.g., quinidine, procainamide, amiodarone and sotalol) or might increase the risk of heart rhythm problems when used with some other drugs(e.g., methadone (used for pain relief and part of drug addiction detoxification), moxifloxacin (an antibiotic), antipsychotics used for serious mental illnesses).

Pregnancy and breast-feeding

ELIGARD is not intended for women.
Driving and using machines

Fatigue, dizziness and visual disturbances are possible side effects of the treatment with ELIGARD or might be a result from the disease. If you suffer from these side effects, take care when driving or operating machines.

3. HOW SHOULD YOU USE THE MEDICINE?

Dose

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure about the dosage and manner of treatment with the medicine.

Dosage and manner of treatment will be determined by the doctor only. Usual dose for ELIGARD 22.5 mg is administration **once** every **three months**.

The injected solution forms an active substance depot from which a continuous release of the active substance leuprorelin acetate takes place over a period of three months.

Additional tests

Response to therapy with ELIGARD should be checked by your doctor by means of checking specific clinical values and by measuring the blood levels of the **PSA** (prostate-specific antigen).

Method of administration

ELIGARD should only be administered by your **doctor** or **a nurse.** They will also take care of the preparation of the solution for injection (according to the instructions given in *Section 7 Information for Healthcare Professionals*, at the end of this leaflet).

After preparation, ELIGARD is administered as a subcutaneous injection (injection into the tissue below the skin). Intra-arterial (into an artery) or intravenous (into a vein) injection has to be strictly avoided. As with other active substances that are injected subcutaneously, the site of injection should be varied periodically.

If you accidentally have taken a higher dose

Since the injection is generally administered by your doctor or appropriately trained staff, overdosage is not to be expected.

If a larger amount than intended is nevertheless administered, your doctor will monitor you specifically and give you additional treatment as required.

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

If you forgot to take the medicine

Please talk to your doctor if you believe that your three monthly administration of ELIGARD was forgotten.

If you stop taking the medicine

As a general rule, the therapy of prostate cancer with ELIGARD requires long-term treatment. Therefore, therapy should not be terminated, even if there is an improvement in the symptoms or if they disappear completely.

If the treatment with ELIGARD is stopped prematurely, a deterioration of disease-related symptoms can occur.

You should continue treatment as recommended by your doctor

Even if there is an improvement in your health, you should not stop the therapy without consulting the doctor.

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

4. SIDE EFFECTS

As with any medicine, the use of ELIGARD may cause side effects in some users. Do not be alarmed by reading the list of side effects. It is possible you will not suffer any of them.

Side effects that have been observed during treatment with ELIGARD are mainly attributable to the specific effect of the active substance leuprorelin acetate, namely the increase and decrease of certain hormones. The most commonly described side effects are hot flashes (approximately 58% of patients), nausea, malaise and fatigue, as well as temporary local irritations at the site of injection.

Side effects occurring at the beginning of treatment

During the first weeks of treatment with ELIGARD, disease-specific symptoms may worsen, because in first instance there is generally a brief increase in the male sex hormone testosterone in the blood. Therefore, your doctor may administer an appropriate anti-androgen (substance that inhibits the effect of testosterone) at the initial phase of the treatment in order to reduce possible after-effects *(See also Section 2 Before using the medicine - "Complications due to initial treatment with ELIGARD")*.

Local side effects

Local side effects that have been described after the injection of ELIGARD are typically those, which are often associated with similar subcutaneously injected preparations (preparations which are injected into the tissue below the skin). Mild burning immediately after the injection is very common. Stinging and pain after the injection are common, as well as a bruise at the injection site. Redness of the skin at the injection site has been reported commonly. Tissue hardening and ulceration are uncommon.

These local side effects following subcutaneous injection are mild and described as being of brief duration. They do not occur again in between the individual injections.

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

- Hot flashes
- Spontaneous bleeding in skin or mucous membrane, redness of the skin
- Fatigue, injection-related side effects *(see also local side effects above)*

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

- Nasopharyngitis (symptoms of common cold)
- Nausea, malaise, diarrhoea, inflammation of the stomach and intestines (gastroenteritis/colitis)
- Itching, nightly sweating
- Pain in the joints
- Irregular trips to the toilet to pass water (also at night), difficulty in starting to pass water, painful urination, reduced urine output
- Breast tenderness, swelling of the breast, shrinking of testicles, testicular pain, infertility, erectile dysfunction, reduced penis size

- Rigors (episodes of exaggerated shaking with high fevers), weakness
- Prolonged bleeding time, changes in blood values, decreased red blood cells/low red blood cell count

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

- Urinary tract infection, local skin infection
- Worsening of diabetes mellitus
- Abnormal dreams, depression, decreased libido
- Dizziness, headache, an alteration in the skin sensation, insomnia, taste disturbance, smell disturbance
- Hypertension (increased blood pressure), hypotension (decreased blood pressure)
- Shortness of breath
- Constipation, dry mouth, dyspepsia (disturbed digestion, with symptoms as full stomach, pain in the stomach, belching, nausea, vomiting, burning feeling in the stomach), vomiting
- Clamminess, increased sweating
- Back pain, muscles cramps
- Haematuria (blood in the urine)
- Bladder spasm, more trips to the toilet to pass water than usual, unable to pass water
- Enlargement of male breast tissue, impotence
- Lethargy (sleepiness), pain, fever
- Increased weight
- Loss of balance, light-headedness
- Muscle wasting/loss of muscle tissue after prolonged use

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

- Abnormal involuntary movements
- Sudden loss of consciousness, fainting
- Flatulence, belching
- Hair loss, skin eruption (pimples on the skin)
- Breast pain
- Injection site ulceration

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

- Injection site necrosis

Not known (frequency cannot be estimated from the available data)

- Changes in ECG [Electrocardiogram] (QT prolongation)
- Inflammation of lungs, lung disease
- Idiopathic intracranial hypertension (increased intracranial pressure around the brain characterised by headache, double vision and other visual symptoms and ringing or buzzing in one or both ears)
- Reddish non-elevated, target-like or circular patches on the trunk, often with central blisters, skin peeling, ulcers of mouth, throat, nose, genitals and eyes. These serious skin rashes can be preceded by fever and flu-like symptoms (Stevens-Johnson syndrome/Toxic Epidermal Necrolysis)
- Skin redness and itchy rash (Toxic skin eruption)
- A skin reaction that causes red spots or patches on the skin, that may look like a target or "bulls-eye" with a dark red centre surrounded by paler red rings (Erythema Multiforme)

Other side effects

Other side effects that have been described in the literature in relation with treatment with leuprorelin, the active substance of ELIGARD, are oedema (accumulation of fluid in tissue, appearing as swelling of the hands and feet), pulmonary embolism (resulting in symptoms like breathlessness, difficulty in breathing and chest pain)**,** palpitations (awareness of your heartbeat), muscle weakness, chills, rash, impaired memory and impaired vision. Increasing signs of a decrease in bone tissue (osteoporosis) may be expected after long-term treatment with ELIGARD. Due to osteoporosis, the risk for fractures increases.

Serious allergic reactions, which cause difficulty in breathing or dizziness, have been reported rarely after administration of products in the same class as ELIGARD.

Seizures have been reported after administration of products in the same class as ELIGARD.

If a side effect occurred, if one of the side effects worsens or when you experience a side effect that is not mentioned in the leaflet, you should consult with the doctor.

Reporting of side effects

Side effects can be reported to the Ministry of Health through a link "reporting of side effects due to drug therapy" located in the home page of the Ministry of Health website (www.health.gov.il) which refers to an online form for reporting side effects, or by accessing the following link: https://sideeffects.health.gov.il
Additionally, you may also report to Kamada Ltd. to email address: pharmacovigilance@kamada.com

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine and any other medicine must be kept in a safe place out of the reach and sight of children and/or infants and thereby prevent poisoning. Do not induce vomiting without an explicit instruction from the doctor.
Do not use this medicine after the expiry date (exp. date) which is indicated on the packaging. The expiry date refers to the last day of that month.

Storage instructions

Store in a refrigerator at 2°C - 8°C.
Store in the original package in order to protect from moisture.

This product must be at room temperature prior to injection. Remove from the refrigerator approximately 30 minutes before use. Once outside the refrigerator this product may be stored in its original packaging below 25°C for up to four weeks. Afterward dispose of the product. Do not return to refrigerator.

Once the tray has been opened, the product must be prepared straight away and the product must be used immediately. For single use only.

Instructions on disposal of unused or expired ELIGARD packs

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. ADDITIONAL INFORMATION

Syringe B contains powder of active substance.
Solvent syringe (syringe A) contains:
75:25 Poly (DL-lactide-co-glycolide) and N-methyl-2-pyrrolidone

What the medicine looks like and contents of the pack?

ELIGARD is a powder and solvent for solution for injection.

ELIGARD 22.5 mg is available in the following packs:

- A thermoformed tray pack consisting of two thermoformed trays in a cardboard carton. One tray contains syringe A, a large plunger rod for syringe B and a desiccant pouch. The other tray contains syringe B, a 20 gauge sterile needle and a desiccant pouch.

License holder and his address
Kamada Ltd., Beit Kama

Revised in December 2024.

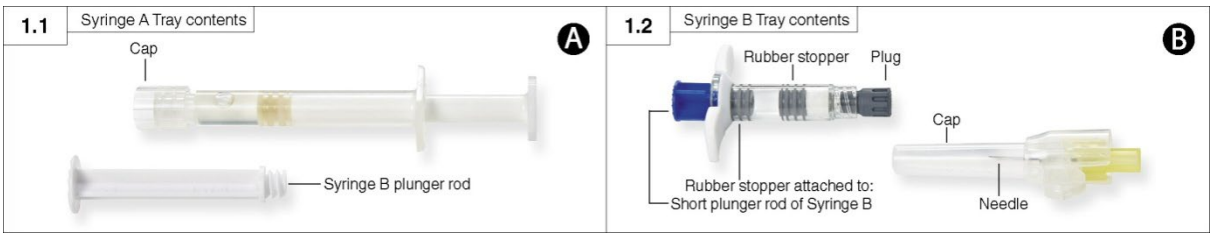
Registration number of the medicine in the National Drug Registry of the Ministry of Health:
156-79-33678

7. INFORMATION FOR HEALTHCARE PROFESSIONALS

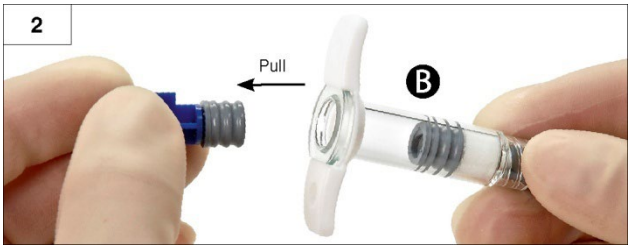
The following information is intended for healthcare professionals only:

Allow the product to come to room temperature by removing from the refrigerator approximately 30 minutes prior to use.
Please prepare the patient for injection first, followed by the preparation of the product, using the instructions below. If the product is not prepared using the proper technique, it should not be administered as lack of clinical efficacy may occur due to incorrect reconstitution of the product.

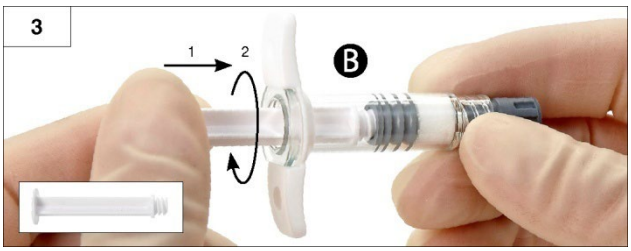
Step 1: Open both trays (tear off the foil from the corner which can be recognized by a small bubble) and empty the contents onto a clean field (two trays containing Syringe A (Figure 1.1) and Syringe B (Figure 1.2)). Discard the desiccant pouches.



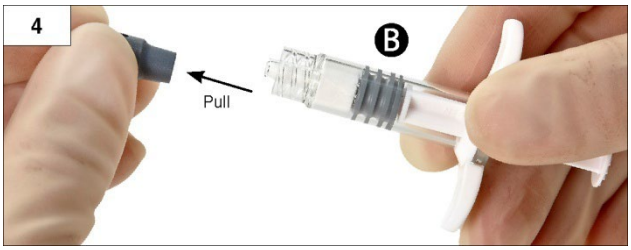
Step 2: **<u>Pull out</u>** and **do not unscrew** the blue coloured short plunger rod together with the attached grey stopper from Syringe B and discard (Figure 2). **Do not attempt to mix the product with two stoppers in place.**



Step 3: Gently screw the Syringe B white plunger rod to the remaining grey stopper in Syringe B (Figure 3).

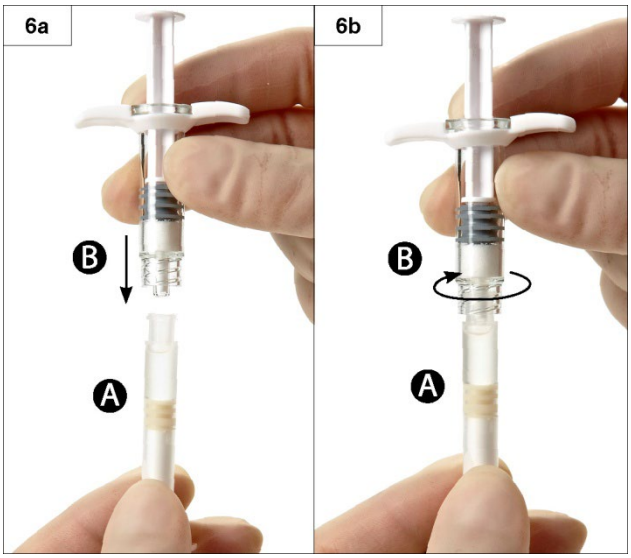


Step 4: Remove the grey rubber cap from Syringe B and put down the Syringe (Figure 4).

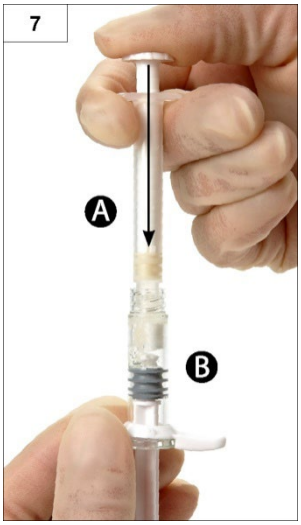


Step 5: Hold Syringe A in a vertical position to ensure no liquid leaks out and unscrew the clear cap from Syringe A (Figure 5).

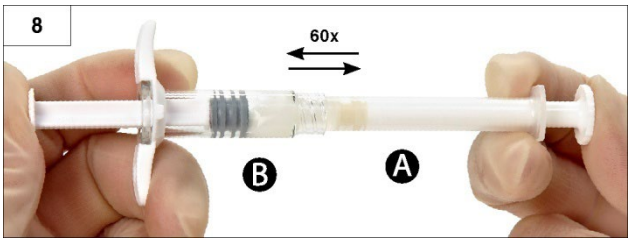
Step 6: Join the two syringes together by pushing in and twisting Syringe B onto Syringe A until secure (Figure 6a and 6b). **Do not over tighten**.



Step 7: Flip the connected unit over and continue to hold the syringes vertically with Syringe B on the bottom while injecting the liquid contents of Syringe A into Syringe B containing the powder (leuproreline acetate) (Figure 7).



Step 8: Thoroughly mix the product by gently pushing the contents of both syringes back and forth between syringes (60 times in total, which takes approximately 60 seconds) in a horizontal position to obtain a homogenous, viscous solution (Figure 8). Do not bend the syringe system (please note that this may cause leakage as you may partially unscrew the syringes).

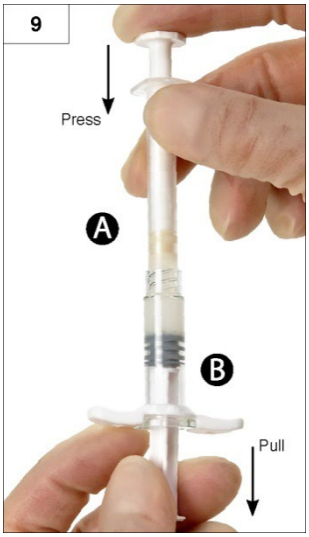


When thoroughly mixed, the viscous solution will appear with a colour in the range of colourless to white to pale yellow (which could include shades of white to pale yellow).

Important: After mixing proceed with the next step immediately as the product gets more viscous over time. Do not refrigerate the mixed product.

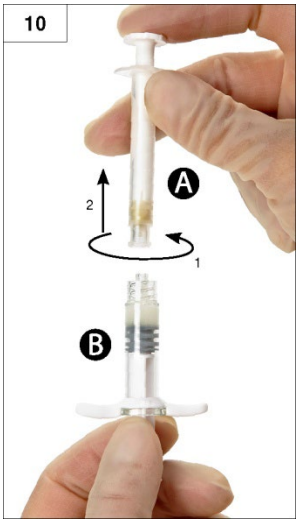
Please note: Product must be mixed as described; shaking **WILL NOT** provide adequate mixing of the product.

Step 9: Hold the syringes vertically with Syringe B on the bottom. The syringes should remain securely coupled. Draw the entire mixed product into Syringe B (short, wide syringe) by pushing down the Syringe A plunger and slightly withdrawing the Syringe B plunger (Figure 9).



Step 10: Twist off Syringe A while continuing to push down on the Syringe A plunger (Figure 10). Ensure that no product leaks out as the needle will then not secure properly when attached.

Please note: one large or a few small air bubbles may remain in the formulation - this is acceptable. **Please do not purge the air bubbles from Syringe B at this stage as product may be lost!**

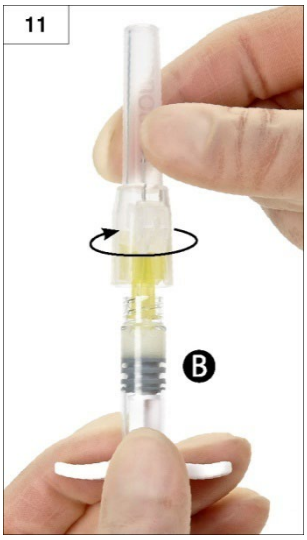


Step 11:
- Hold Syringe B upright and hold back the white plunger to prevent loss of the product.
- Open pack of the safety needle by peeling back paper tab and take out safety needle.
- Secure the safety needle to Syringe B by holding the syringe and gently turning the needle clockwise with approximately a three-quarter turn until the needle is secure (Figure 11).

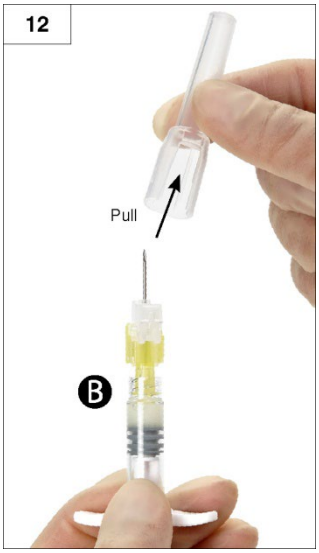
Do not over tighten as this may cause cracking of the needle hub resulting in leakage of the product during injection.

Should the needle hub crack, appear to be damaged, or have any leakage, the product should not be used. The damaged needle should not be substituted/replaced and the product should not be injected. The entire product should be disposed of securely.

In the event of damage to the needle hub, a new replacement product should be used.



Step 12: Pull off the protective needle cover prior to administration (Figure 12).
Important: Do not operate the safety needle mechanism before administration.

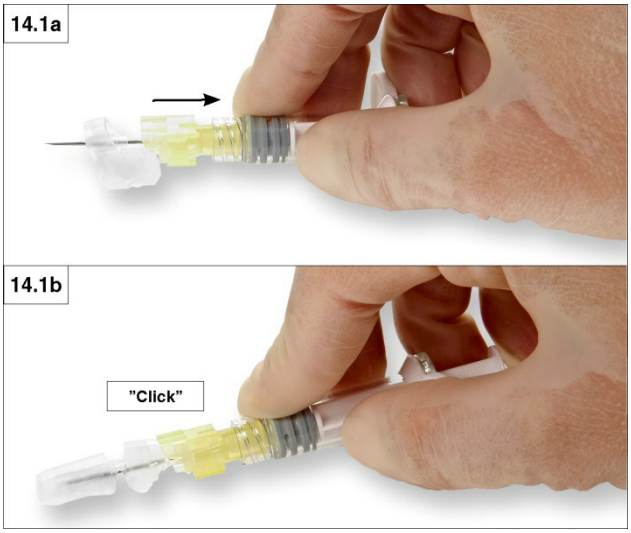


Step 13: Prior to administration, purge any large air bubbles from Syringe B. Administer the product subcutaneously. Please ensure that the full amount of the product in Syringe B is injected.

Step 14: After injection, lock the safety shield using any of the activation methods listed below.

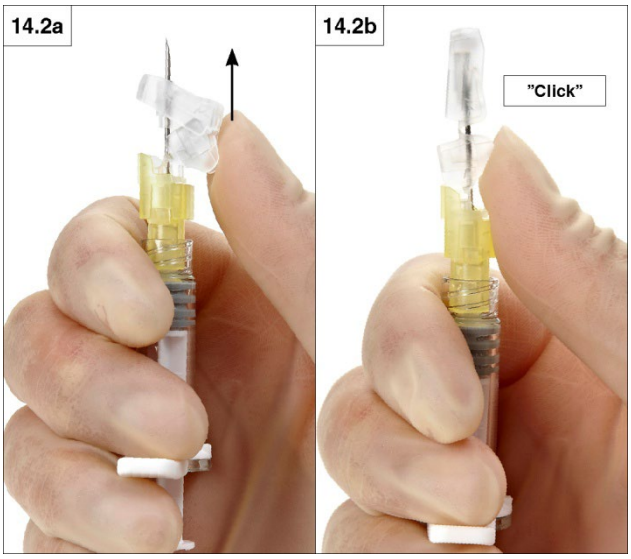
1. **Closure on a flat surface**

Press the safety shield, lever side down, onto a flat surface (Figure 14.1a and b) to cover the needle and lock the shield.
Verify locked position through audible and tactile “click”. Locked position will completely cover needle tip (figure 14.1b).



2. **Closure with your thumb**

Placing your thumb on the lever, slide the safety shield toward the needle tip (Figure 14.2a and b) to cover the needle and lock the shield.
Verify locked position through audible and tactile “click”. Locked position will completely cover needle tip (figure 14.2b).



Step 15: Once safety shield is locked, immediately dispose of the needle and syringe in an approved sharps container.