PATIENT INFORMATION LEAFLET

ELIGARD® 22.5 mg
Powder and solvent for solution for injection
Leuprorelin acetate

Read all of this leaflet carefully before you start using this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT ELIGARD® IS AND WHAT IT IS USED FOR

The active substance of ELIGARD belongs to the group of so-called gonadotropin releasing hormones. These medicines are used to decrease the production of certain sex hormones (testosterone).

ELIGARD is used to treat hormone dependent advanced **prostate cancer** in adult men.

2. BEFORE YOU USE ELIGARD®

Do not use ELIGARD
- 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.
- 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.

Take special care with 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.

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

Using other medicines
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

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 TO USE ELIGARD®

ELIGARD should always be used exactly as your doctor has told you.

Dosage
If not otherwise prescribed by your doctor, ELIGARD 22.5 mg is administered **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 so-called prostate-specific antigen (PSA).

Method of administration
ELIGARD will usually be administered by your **doctor** or **a nurse**. They will also take care of the preparation of the ready-to-use solution (according to the instructions given in the separate *technical leaflet*). In case the ready-to-use solution will be prepared by yourself, please consult your doctor for detailed instructions on the procedure.

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 receive more ELIGARD than you should
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 the administration of ELIGARD is forgotten
Please talk to you doctor if you believe that your three monthly administration of ELIGARD was forgotten.

Effects when the treatment with ELIGARD is stopped
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 not stop the therapy prematurely without previously consulting your doctor.

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

4. POSSIBLE SIDE EFFECTS

Like all medicines, ELIGARD can cause side effects, although not everybody gets 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.

Initial side effects
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 you use ELIGARD, Initial treatment complications*).

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 (affects more than 1 user in 10)
- 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 (affects 1 to 10 users in 100)
- Nasopharyngitis (symptoms of common cold)
- Nausea, malaise,diarrhoea,
- 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
- Rigors (episodes of exaggerated shaking with high fevers), weakness
- Prolonged bleeding time, changes in blood values

Uncommon side effects (affects 1 to 10 users in 1,000)
- Urinary tract infection, local skin infection
- Worsening of diabetes mellitus
- Abnormal dreams, depression, decreased libido
- Dizziness, headache, an alteration in 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 such 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

Rare side effects (affects 1 to 10 users in 10,000)
- 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 (affects less than 1 user in 10,000)
- Injection site necrosis

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.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE ELIGARD®

Keep out of the reach and sight of children.

Do not use after the expiry date printed on the outer packaging.

Storage instructions:
Store in a refrigerator at 2°C - 8°C.
Store in the original container in order to protect from moisture.

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. FURTHER INFORMATION

What ELIGARD contains
The active substance is leuprorelin acetate.
One pre-filled syringe (Syringe B) contains 22.5 mg leuprorelin acetate.

The other ingredients are Poly(DL-lactic-co-glycolic-acid) (75:25) and N-methyl-2-pyrrolidone in the pre-filled syringe with solution for injection (Syringe A).

What ELIGARD 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 pre-filled syringe A, a large plunger rod for syringe B and a desiccant pouch. The other tray contains pre-filled syringe B, a 20-gauge sterile needle and a desiccant pouch.
- A bundle pack containing kits of 2 x 2 pre-filled syringes (1 x Syringe A; 1 x Syringe B)

Not all pack sizes may be available.

This leaflet was last revised in January 2014.

Marketing Authorisation Holder
Astellas Pharma Europe B.V.
Sylviusweg 62
2333 BE Leiden
The Netherlands

Manufacturers
Tolmar Inc.
701 Centre Avenue
Ft. Collins, CO 80526
USA

Cangene bioPharma Inc.
1111 South Paca Street
Baltimore, MD 21230
USA

Manufacturer responsible for batch release

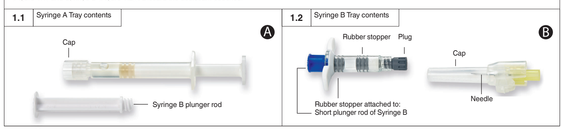
Manufacturing license holder
Astellas Pharma Europe B.V.
Sylviusweg 62
2333 BE Leiden
The Netherlands

Manufacturing site
Astellas Pharma Europe B.V.
Hogemaat 2
7942 JG Meppel
The Netherlands

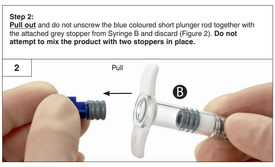
7. INFORMATION FOR HEALTHCARE PROFESSIONALS

Allow the product to come to room temperature.
Please prepare the patient for injection first, followed by the preparation of the product, using the instructions below.

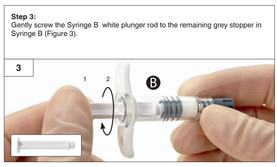
Step 1:
Open both trays (tear off the foil from the corner which can be recognized by a small bubble) and empty the contents onto a clean field (two trays containing Syringe A (Figure 1.1) and Syringe B (Figure 1.2)). Discard the desiccant pouches.



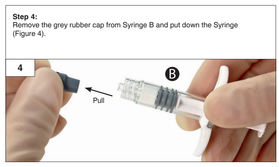
Step 2:
Pull out and do not unscrew the blue coloured short plunger rod together with the attached grey stopper from Syringe B and discard (Figure 2). **Do not attempt to mix the product with two stoppers in place.**



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

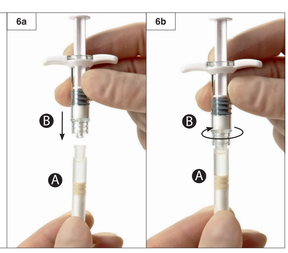


Step 4:
Remove the grey rubber cap from Syringe B and put down the Syringe (Figure 4).

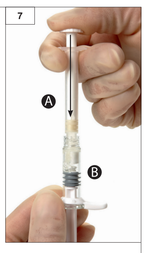


Step 5:
Hold Syringe A in a vertical position to ensure no liquid leaks out and unscrew the clear cap from Syringe A (Figure 5).

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 (leuprorelin acetate) (Figure 7).

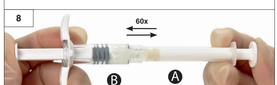


Step 8:
Thoroughly mix the product by gently pushing the contents of both syringes back and forth between syringes (60 times in total, which takes approximately 60 seconds) in a horizontal position to obtain a homogenous, viscous solution (Figure 8). Do not bend the syringe system (please note that this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

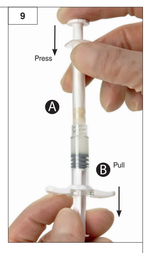
When thoroughly mixed, the viscous solution will appear with a colour in the range of colourless to white to pale yellow (which could include shades of white to pale yellow).

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.

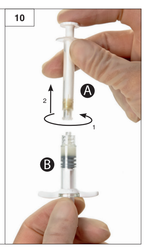


Step 9:
Hold the syringes vertically with Syringe B on the bottom. The syringes should remain securely coupled. Draw the entire mixed product into Syringe B (short, wide syringe) by pushing down the Syringe A plunger and slightly withdrawing the Syringe B plunger (Figure 9).

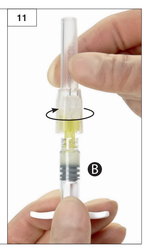


Step 10:
Twist off Syringe A while continuing to push down on the Syringe A plunger (Figure 10). Ensure that no product leaks out as the needle will then not secure properly when attached.

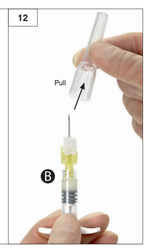
Please note: one large or a few small air bubbles may remain in the formulation - this is acceptable. **Please do not purge the air bubbles from Syringe B at this stage as product may be lost!**



Step 11:
Hold Syringe B upright. 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 twisting the needle clockwise to fully seat the needle (Figure 11).
Do not over tighten.



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.