**ELIGARD 7.5 mg**
**ELIGARD 22.5 mg**
**ELIGARD 45 mg**

## 1. NAME OF THE MEDICINAL PRODUCT

ELIGARD 7.5 mg powder and solvent for solution for injection

ELIGARD 22.5 mg powder and solvent for solution for injection

ELIGARD 45 mg powder and solvent for solution for injection

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ELIGARD 7.5 mg
One prefilled syringe with powder for solution for injection contains 7.5 mg leuprorelin acetate, equivalent to 6.96 mg leuprorelin.

ELIGARD 22.5 mg
One prefilled syringe with powder for solution for injection contains 22.5 mg leuprorelin acetate, equivalent to 20.87 mg leuprorelin.

ELIGARD 45 mg
One prefilled syringe with powder for solution for injection contains 45 mg leuprorelin acetate, equivalent to 41.7 mg leuprorelin.

For *a full list of* excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Powder and solvent for solution for injection**,**

Powder (Syringe B):
Pre-filled syringe with a white to off-white powder.

Solvent (Syringe A):
Pre-filled syringe with a clear, colourless to pale yellow solution

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

ELIGARD is indicated for the treatment of hormone dependent advanced prostate cancer

## 4.2 Posology and method of administration

Dosage for Adult Males

ELIGARD should be administered under the direction of a healthcare professional having available the appropriate expertise for monitoring the response to treatment.

ELIGARD 7.5 mg is administered as a single subcutaneous injection every month. The injected solution forms a solid medicinal product delivery depot and provides continuous release of leuprorelin acetate for one month.

ELIGARD 22.5 mg is administered as a single subcutaneous injection every three months. The injected solution forms a solid medicinal product delivery depot and provides continuous release of leuprorelin acetate over a three-month period.

ELIGARD 45 mg is administered as a single subcutaneous injection every six months. The injected solution forms a solid medicinal product delivery depot and provides continuous release of leuprorelin acetate over a six-month period.

As a rule, therapy of advanced prostate cancer with ELIGARD entails long-term treatment and therapy should not be discontinued when remission or improvement occurs.

Response to ELIGARD should be monitored by clinical parameters and by measuring prostate specific antigen (PSA) serum levels. Clinical studies have shown that testosterone levels increased during the first 3 days of treatment in the majority of non-orchiectomised patients and then decreased to below medical castration levels within 3 - 4 weeks. Once attained, castrate levels were maintained as long as medicinal product therapy continued (< 1% testosterone breakthroughs). In case the patient's response appears to be sub-optimal, it should be confirmed that serum testosterone levels have reached or are remaining at castrate levels.

Administration

The contents of the two pre-filled sterile syringes must be mixed immediately prior to administration of ELIGARD by subcutaneous injection.

Regarding the mixing procedure, see section 6.4. Lack of clinical efficacy may occur due to incorrect reconstitution of the product.

Based on data from animal experience, intra-arterial or intravenous injection, respectively, has to be strictly avoided.

As with other medicinal products administered by subcutaneous injection, the injection site should be varied periodically.

Children and adolescents

There is no experience in children (under the age of 18 years) (see also section 4.3)

Dose Adjustment in Specific Patient Populations
No clinical studies were performed in patients with either liver or kidney impairment.

## 4.3 Contraindications

Hypersensitivity to leuprorelin acetate, to other GnRH agonists or to any of the excipients.

In patients who previously underwent orchiectomy (as with other GnRH agonists, ELIGARD does not result in further decrease of serum testosterone in case of surgical castration).

As sole treatment in prostate cancer patients with spinal cord compression or evidence of spinal metastases (see also section 4.4)

ELIGARD is contraindicated in women and in paediatric patients.

## 4.4 Special warnings and special precautions for use

Leuprorelin acetate, like other GnRH agonists, causes a transient increase in serum concentrations of testosterone, dihydrotestosterone and acid phosphatase during the first week of treatment. Patients may experience worsening of symptoms or onset of new symptoms, including bone pain, neuropathy, haematuria, or ureteral or bladder outlet obstruction (see section 4.8). These symptoms usually subside on continuation of therapy.

Additional administration of an appropriate antiandrogen should be considered beginning 3 days prior to leuprorelin therapy and continuing for the first two to three weeks of treatment. This has been reported to prevent the sequelae of an initial rise in serum testosterone.

Following surgical castration, ELIGARD does not lead to a further decrease in serum testosterone levels in male patients.

Cases of ureteral obstruction and spinal cord compression, which may contribute to paralysis with or without fatal complications, have been reported with GnRH agonists. If spinal cord compression or renal impairment develops, standard treatment of these complications should be instituted.

Patients with vertebral and/or brain metastases as well as patients with urinary tract obstruction should be closely monitored during the first few weeks of therapy.

A proportion of patients will have tumors which are not sensitive to hormone manipulation. Absence of clinical improvement despite adequate testosterone suppression is diagnostic of this condition, which will not benefit from further therapy with ELIGARD.

Decreased bone density has been reported in the medical literature in men who have had orchiectomy or who have been treated with a GnRH agonist (see section 4.8).
Antiandrogen therapy significantly increases the risk for fractures owing to osteoporosis. Only limited data is available on this issue. Fractures owing to osteoporosis were observed in 5% of patients following 22 months of pharmacological androgen deprivation therapy and in 4% of patients following 5 to 10 years of treatment. The risk for fractures owing to osteoporosis is generally higher than the risk for pathological fractures.

Apart from long lasting testosterone deficiency, increased age, smoking and consumption of alcoholic beverages, obesity and insufficient exercise may have an influence on the development of osteoporosis.

During post-marketing surveillance, rare cases of pituitary apoplexy (a clinical syndrome secondary to infarction of the pituitary gland) have been reported after the administration of GnRH-agonists, with a majority occurring within 2 weeks of the first dose, and some within the first hour. In these cases, pituitary apoplexy was presented as sudden headache, vomiting, visual changes, ophthalmoplegia, altered mental status, and sometimes cardiovascular collapse. Immediate medical attention is required.

Androgen deprivation therapy may prolong the QT interval. Providers should consider whether the benefits of androgen deprivation therapy outweigh the potential risks in patients with congenital long QT syndrome, congestive heart failure, frequent electrolyte abnormalities, and in patients taking drugs known to prolong the QT interval. Electrolyte abnormalities should be corrected. Consider periodic monitoring of electrocardiograms and electrolytes.

Increased risk of developing myocardial infarction, sudden cardiac death and stroke has been reported in association with use of GnRH agonists in men. The risk appears low based on the reported odds ratios, and should be evaluated carefully along with cardiovascular risk factors when determining a treatment for patients with prostate cancer. Patients receiving a GnRH agonist should be monitored for symptoms and signs suggestive of development of cardiovascular disease and be managed according to current clinical practice.

Changes in glucose tolerance have been reported in some patients receiving GnRH agonist therapy. Hyperglycemia may represent development of diabetes mellitus or worsening of glycemic control in patients with diabetes. Monitor blood glucose and/or glycosylated hemoglobin (HbA1c) periodically in patients receiving a GnRH agonist and manage with current practice for treatment of hyperglycemia or diabetes.

Post marketing reports of convulsions have been observed in patients on leuprorelin acetate therapy with or without a history of predisposing factors. Convulsions are to be managed according to the current clinical practice.

There have been postmarketing reports of interstitial pneumonitis associated with leuprorelin use. Treatment should be discontinued immediately if the patient develops any signs or symptoms suggestive of interstitial lung disease.

## 4.5 Interaction with other medicinal products and other forms of interaction

No pharmacokinetic drug-drug interaction studies have been performed with ELIGARD. There have been no reports of any interactions of leuprorelin acetate with other medicinal products.

## 4.6 Pregnancy and lactation

Not applicable as ELIGARD is contraindicated in women.

## 4.7 Effects on ability to drive and use machines

No studies on the effects of ELIGARD on the ability to drive and use machines have been performed.
The ability to drive and operate machines may be impaired due to fatigue, dizziness and visual disturbances being possible side effects of treatment or resulting from the underlying disease.

## 4.8 Undesirable effects

Adverse reactions seen with ELIGARD are mainly subject to the specific pharmacological action of leuprorelin acetate, namely increases and decreases in certain hormone levels. The most commonly reported adverse reactions are hot flashes, malaise, nausea and fatigue and transient local irritation at the site of injection. Mild or moderate hot flashes occur in approximately 58% of patients.

The following adverse events were reported during clinical trials with ELIGARD in patients with advanced prostate carcinoma. Adverse events are classified, by frequency, as very common (≥1/10), common (≥1/100, <1/10), uncommon (≥1/1,000, <1/100), rare (≥1/10,000, <1/1,000), and very rare (<1/10,000), not known (cannot be estimated from the available data).

*Table 1*: ***Undesirable effects in clinical studies with Eligard***

| | |
|---|---|
| **Infections and infestations** | |
| common | nasopharyngitis |
| uncommon | urinary tract infection, local skin infection |
| **Metabolism and nutrition disorders** | |
| uncommon | aggravated diabetes mellitus |
| **Psychiatric disorders** | |
| uncommon | abnormal dreams, depression, decreased libido |
| **Nervous system disorders** | |
| uncommon | dizziness, headache, hypoaesthesia, insomnia, taste disturbance, smell disturbance, vertigo |
| rare | abnormal involuntary movements |
| **Vascular disorders** | |
| very common | hot flashes |
| uncommon | hypertension, hypotension |
| rare | syncope, collapse |
| **Respiratory, thoracic and mediastinal disorders** | |
| uncommon | rhinorrhoea, dyspnoea |
| not known | interstitial lung disease |
| **Gastrointestinal disorders** | |
| common | nausea, diarrhea, gastroenteritis/colitis |
| uncommon | constipation, dry mouth, dyspepsia, vomiting |
| rare | flatulence, eructation, |

| | |
|---|---|
| **Skin and subcutaneous tissue disorders** | |
| very common | ecchymoses, erythema |
| common | pruritus, night sweats |
| uncommon | clamminess, increased sweating |
| rare | alopecia, skin eruption |
| **Musculoskeletal, connective tissues and bone disorders** | |
| common | arthralgia, limb pain, myalgia |
| uncommon | back pain, muscle cramps |
| **Renal and urinary disorders** | |
| common | urinary infrequency, difficulty in micturation, dysuria, nocturia, oliguria |
| uncommon | bladder spasm, haematuria, aggravated urinary frequency, urinary retention |
| **Reproductive system and breast disorders** | |
| common | breast tenderness, testicular atrophy, testicular pain infertility, breast hypertrophy, erectile dysfunction, reduced penis size |
| uncommon | gynaecomastia, impotence, testicular disorder |
| rare | breast pain |
| **General disorders and administration site reactions** | |
| very common | fatigue, injection site burning, injection site paraesthesia |
| common | malaise, injection site pain, injection site bruising, injection site stinging , rigors, weakness |
| uncommon | injection site pruritus, injection site induration, lethargy, pain, pyrexia |
| rare | injection site ulceration |
| very rare | injection site necrosis |
| **Blood and lymphatic system disorders** | |
| Common | hematology changes, anaemia |
| **Investigations** | |
| common | increased blood creatinine phosphokinase, prolonged coagulation time |
| uncommon | increased alanine aminotransferase, increased blood triglycerides, prolonged prothrombin time, increased weight |

Other adverse events which have been reported in general to occur with leuprorelin acetate treatment include peripheral oedema, pulmonary embolism, palpitations, myalgia, muscle weakness, an alteration in the skin sensation, chills, peripheral vertigo, rash, amnesia and visual disturbances. Muscular atrophy has been observed with long term use of products in this class. Infarction of pre-existing pituitary apoplexy has been reported rarely after administration of both short and long acting GnRH agonists. There have been rare reports of thrombocytopenia and leucopenia. Changes in glucose tolerance have been reported.

Convulsions have been reported after GnRH agonist analogue administration (see section 4.4).

Local adverse events reported after injection of ELIGARD are similar to the local adverse events associated with similar subcutaneously injected products.

Generally, these localised adverse events following subcutaneous injection are mild and described as being of brief duration.

Anaphylactic/anaphylactoid reactions have been reported rarely after GnRH agonist analogue administration.

Changes in Bone Density
Decreased bone density has been reported in the medical literature in men who have had orchiectomy or who have been treated with a GnRH analogues. It can be anticipated that long periods of treatment with leuprorelin may show increasing signs of osteoporosis. Regarding the increased risk for fractures owing to osteoporosis (see section 4.4).

Exacerbation of signs and symptoms of the disease
Treatment with leuprorelin acetate can cause exacerbations of signs and symptoms of the disease during the first few weeks. If conditions such as vertebral metastases and/or urinary obstruction or haematuria are aggravated, neurological problems, such as weakness and/or paraesthesia of the lower limbs or worsening of urinary symptoms may occur.

### 4.9 Overdose

ELIGARD does not have the potential for abuse, and deliberate overdose is unlikely. There are no reports of abuse or overdose having occurred in clinical practice with leuprorelin acetate, but in the event that excessive exposure becomes a reality, observation and symptomatic supportive treatment are recommended.

## 5. PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Gonadotropin releasing hormone analogues
ATC code: L02A E02

Leuprorelin acetate is a synthetic nonapeptide agonist of naturally occurring gonadotropin releasing hormone (GnRH) that, when given continuously, inhibits pituitary gonadotropin secretion and suppresses testicular steroidogenesis in males. This effect is reversible upon discontinuation of medicinal product therapy. However, the agonist possesses greater potency than the natural hormone and the time to recovery of testosterone levels may vary between patients.

Administration of leuprorelin acetate results in an initial increase in circulating levels of luteinising hormone (LH) and follicle stimulating hormone (FSH), leading to a transient increase in levels of the gonadal steroids, testosterone and dihydrotestosterone in males.

Continuous administration of leuprorelin acetate results in decreased levels of LH and FSH. In males, testosterone is reduced to below castrate threshold (≤ 50 ng/dL).

ELIGARD 7.5 mg : These decreases occur within three to five weeks after initiation of treatment. Mean testosterone levels at six months are 6.1 (± 0.4) ng/dL, comparable to levels following bilateral orchiectomy. All patients who received the full dose of 7.5 mg leuprorelin in the pivotal clinical study reached castrate levels at 6 weeks; 94 % had reached this by day 28 and 98% by day 35. In the vast majority of patients the testosterone levels seen were below 20 ng/dL although the full benefit of these low levels has not yet been established. PSA levels decreased by 94% over six months.

ELIGARD 22.5 mg : These decreases occur within three to five weeks after initiation of treatment. Mean testosterone levels at six months are 10.1 (± 0.7) ng/dL, comparable to levels following bilateral orchiectomy. All patients who received the full dose of 22.5 mg leuprorelin in the pivotal clinical study reached castrate levels at 5 weeks; 99 % had reached this by day 28. In the vast majority of patients the testosterone levels seen were below 20 ng/dL although the full benefit of these low levels has not yet been established. PSA levels decreased by 98% over six months.

ELIGARD 45 mg : These decrease occur within three to four weeks after initiation of treatment. Mean testosterone levels at six months are 104 (± 0.53) ng/dL, comparable to levels following bilateral orchiectomy. All but one patient who received the full dose of 45 mg leuprorelin in the pivotal clinical study reached castrate levels at 4 weeks. In the vast majority of patients the testosterone levels seen were below 20 ng/dL although the full benefit of these low levels has not yet been established. PSA levels decreased by 97% over six months

Long-term studies have shown that continuation of therapy maintains testosterone below the castrate level for up to seven years, and presumably indefinitely.

Tumour size was not measured directly during the clinical trial programme, but there was an indirect beneficial tumour response as shown by a 94% reduction in mean PSA for ELIGARD 7.5 mg, 98% reduction for ELIGARD 22.5 mg and 97% reduction for ELIGARD 45 mg.

## 5.2 Pharmacokinetic properties

Absorption:
ELIGARD 7.5 mg:
In patients with advanced carcinoma of the prostate, mean serum leuprorelin concentrations following the initial injection rise to 25.3 ng/ml at 4-8 hr (Cmax) after injection. After the initial increase following each injection (the plateau phase from 2-28 days after each dose), serum concentrations remain relatively constant (0.28 – 1.67 ng/ml). There is no evidence of accumulation during repeated dosing.
ELIGARD 22.5 mg:
In patients with advanced carcinoma of the prostate, mean serum leuprorelin concentrations following the initial injection rise to 127ng/ml at 4.6 hr (Cmax) after injection. After the initial increase following each injection (the plateau phase from 3 - 84 days after each dose), serum concentrations remained relatively constant (0.2 – 2 ng/ml). There is no evidence of accumulation during repeated dosing.

ELIGARD 45 mg:
In patients with advanced carcinoma of the prostate, mean serum leuprorelin concentrations following the initial injection rise to 82 ng/ml at 4.4 hr (Cmax) after injection. After the initial increase following each injection (the plateau phase from 3 - 168 days after each dose), serum concentrations remained relatively constant (0.2 – 2 ng/ml). There is no evidence of accumulation during repeated dosing.

Distribution: The mean steady-state volume of distribution of leuprorelin following intravenous bolus administration to healthy male volunteers was 27 liters. In vitro binding to human plasma proteins ranged from 43% to 49%.

Elimination: In healthy male volunteers, a 1 mg bolus of leuprorelin acetate administered intravenously revealed that the mean systemic clearance was 8.34 l/h, with a terminal elimination half-life of approximately 3 hours based on a two compartment model.

No excretion studies have been conducted with ELIGARD.

No drug metabolism study was conducted with ELIGARD.

### 5.3 Preclinical safety data

Preclinical studies with leuprorelin acetate, revealed in both sexes effects on the reproductive system, which were expected from the known pharmacological properties. These effects were shown to be reversible after discontinuation of the treatment and an appropriate period of regeneration. Leuprorelin acetate did not show teratogenicity. Embryotoxicity/lethality was observed in rabbits, in line with the pharmacological effects of leuprorelin acetate on the reproductive system.

Carcinogenicity studies were performed in rats and mice over 24 months. In rats, a dose-related increase in pituitary apoplexy was observed after subcutaneous administration at doses of 0.6 to 4 mg/kg/day. No such effect was observed in mice.

Leuprorelin acetate and related one-month product ELIGARD 7.5 mg were not mutagenic in a set of in vitro and in vivo assays.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

ELIGARD 7.5 mg
Solvent (syringe A): Poly (DL-lactic-co-glycolic-acid) (50:50)
N-Methylpyrrolidone
ELIGARD 22.5 mg
Solvent (syringe A): Poly (DL-lactic-co-glycolic-acid) (75:25)
N-Methylpyrrolidone
ELIGARD 45 mg
Solvent (syringe A): Poly(DL-lactic-co-glycolic-acid) (85:15)
N-Methylpyrrolidone

Powder (syringe B): None

## 6.2 Incompatibilities

The leuprorelin present in syringe B must only be mixed with the solvent in syringe A and must not be mixed with other medicinal products.

## 6.3 Nature and contents of container

Two pre-filled syringes, one containing powder (Syringe B), and one containing solvent (Syringe A). Together the two syringes comprise a mixing system.

Syringe A has a plunger tip of thermoplastic rubber and is capped with a polyethylene or polypropylene Luer Lock cover. The syringe tip cap is composed of bromobutyl rubber and the two plunger tips of Syringe B are composed of chlorobutyl rubber.

The following pack sizes are available:
ELIGARD 7.5 mg and ELIGARD 22.5 mg:

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

ELIGARD 45 mg
A kit 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 sterile 18-gauge needle and a desiccant pouch.

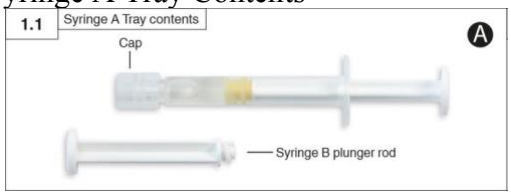
## 6.4 Special precautions for disposal and other handling

Please proceed as follows:
Allow the product to come to room temperature by removing from the refrigerator prior to use.
Please prepare the patient for injection first, followed by the preparation of the product, using the instructions below.

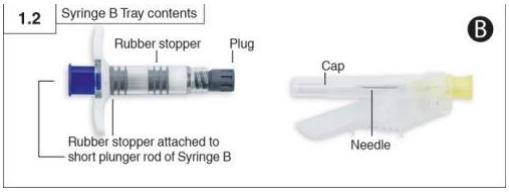
**Step 1:**

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.

a. Syringe A Tray Contents

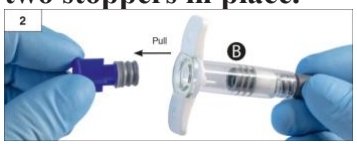



b. Syringe B Tray Contents



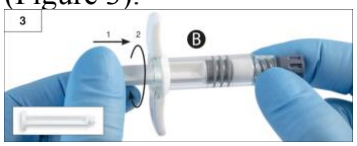

**Step 2:**

**Pull out** and **do not unscrew** the blue colored 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.**



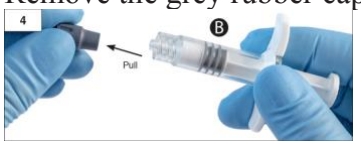

**Step 3:**

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).

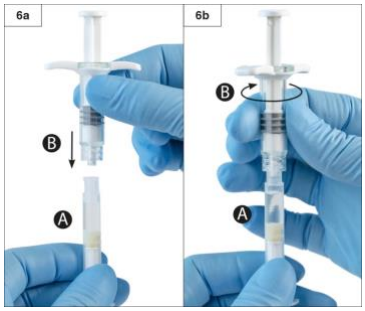



**Step 5:**

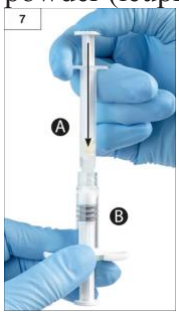
Hold Syringe A in a vertical position to ensure no liquid leaks out and unscrew the clear cap from Syringe A (Figure 5).


**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.**

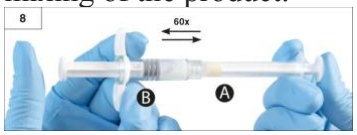



**Step 7:**
Flip the connected unit over and continue to hold the syringes vertically with Syringe B on the bottom while injecting the liquid contents of Syringe A into Syringe B containing the powder (leuprorelin acetate) (Figure 7).

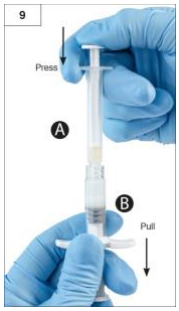



**Step 8:**
Thoroughly mix the product by gently pushing the contents of both syringes back and forth between syringes (60 times in total, which takes approximately 60 seconds) in a horizontal position to obtain a homogenous, viscous solution (Figure 8). Do not bend the syringe system (please note that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

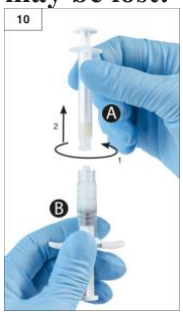



**Step 9:**
Hold the syringes vertically with Syringe B on the bottom. The syringes should remain securely coupled. Draw the entire mixed product into Syringe B (short, wide syringe) by pushing down the Syringe A plunger and slightly withdrawing the Syringe B plunger (Figure 9).




**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 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. Do not remove the hinged safety shield.
- 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** 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**.**

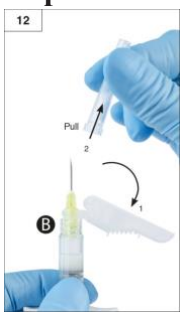
Eligard 7.5 mg/22.5 mg

Eligard 45 mg

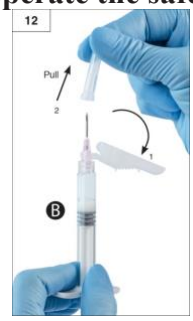
**Step 12:**

Move the safety shield away from the needle and pull off the protective needle cover prior to administration (Figure 12).

**Important: Do not operate the safety needle mechanism before administration.**



Eligard 7.5 mg/22.5 mg



Eligard 45 mg

**Step 13:**

Prior to administration, purge any large air bubbles from Syringe B. Administer the product subcutaneously whilst keeping the safety shield away from the needle. Please ensure that the full amount of the product in Syringe B is injected.

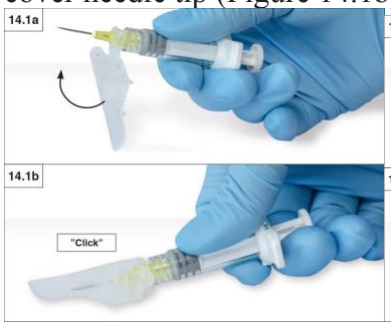
**Step 14:**

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

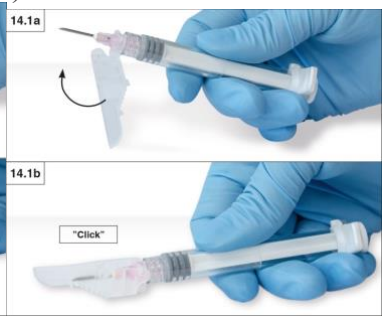
**1. Closure on a flat surface**

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).



Eligard 7.5 mg/22.5 mg

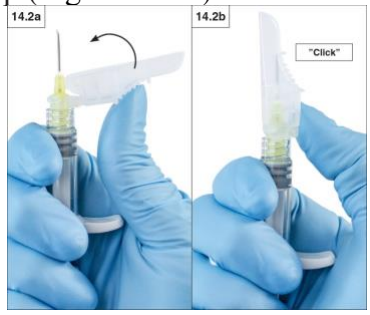


Eligard 45 mg

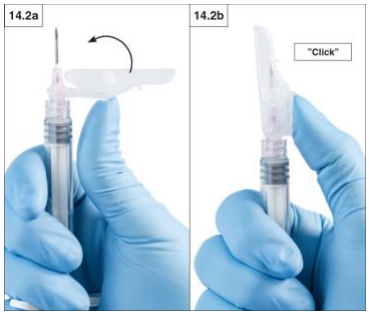
**2. Closure with your thumb**

Placing your thumb on the lever (Figure 14.2a and b), 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).



Eligard 7.5 mg/22.5 mg



Eligard 45 mg

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

**PACKAGING :**

ELIGARD 7.5 mg, 22.5 mg and 45 mg: 1 Box of Syringe A (solvent) + Syringe B (Leuprorelin acetate)

**SHELF LIFE**

2 years

After first opening of the tray or the large outer aluminium pouch, the powder and solvent for solution for injection are to be immediately reconstituted and administered to the patient.

Once reconstituted: use immediately, as the viscosity of the solution increases with time

**STORAGE :**

Store in a refrigerator (2°C – 8°C) in the original package in order to protect from moisture. This product must be at room temperature prior to injection. Remove from the refrigerator before use.

**“HARUS DENGAN RESEP DOKTER”**

**REG NO :**

ELIGARD 7.5 mg powder and solvent for solution for injection :

ELIGARD 22,5 mg powder and solvent for solution for injection :

ELIGARD 45 mg powder and solvent for solution for injection :

**MANUFACTURED BY**
**Tolmar Inc.**
**701 Centre Avenue, Fort Collins, CO 80526, USA.**

**IMPORTED AND MARKETED BY:**
PT. Mitra Pharma Indonesia, Jakarta-Indonesia

**MARKETING AUTHORISATION HOLDER**
PT. Meprofarm Pharmaceutical Industries, Bandung-Indonesia

DISETUJUI OLEH BPOM : 07/03/2024

ID : EREG10025512300114

**Informasi untuk Pasien**
**ELIGARD**
***Leuproline acetate* untuk injeksi**

**Bacalah leaflet ini dengan seksama sebelum anda mengkonsumsi ELIGARD karena leaflet ini mengandung informasi yang penting untuk anda.**
- Simpanlah leaflet ini untuk dibaca kembali.
- Hubungi dokter atau apoteker anda apabila ada pertanyaan lebih lanjut.
- Obat ini diresepkan khusus kepada anda. Dilarang memberikan obat ini kepada orang lain, karena dapat membahayakan bagi orang lain, walaupun gejala dan penyakitnya sama seperti anda.
- Jika anda mengalami efek samping, bicarakan dengan dokter atau apoteker anda. Hal ini termasuk efek samping yang tidak tercantum dalam leaflet ini.

## TENTANG ELIGARD

### Apa kegunaan dari ELIGARD?
ELIGARD digunakan sebagai pengobatan untuk kanker prostat.
ELIGARD harus diberikan oleh tenaga kesehatan profesional.

### Apa itu ELIGARD?
ELIGARD termasuk dalam golongan obat analog *leutinizing hormone-releasing hormone* (analog LH-RH).
ELIGARD bekerja dengan menekan produksi hormon testosteron, hormon alami pria yang dihasilkan oleh testis. Sel-sel pada kanker prostat membutuhkan hormon testosteron untuk pertumbuhannya. Jika jumlah hormon testosteron dalam tubuh menurun, pada umumnya kanker prostat akan mengecil atau berhenti tumbuh, sehingga dapat menurunkan gejala yang berkaitan dengan penyakit tersebut.

### Kapan tidak boleh menggunakan ELIGARD?
- Jika alergi terhadap salah satu dari komponen ELIGARD (lihat bagian zat aktif dan zat tambahan di bawah ini) atau jika pernah mengalami reaksi alergi dengan penggunaan ELIGARD atau obat seperti ELIGARD.
- Jika anda wanita.

**Zat aktif Eligard :** Leuproline acetate

**Zat tambahan Eligard** **:** N-methyl-2-pyrrolidone
Poly (DL-lactide-co-glycolide)

### Seperti apa kemasan ELIGARD?
Kemasan ELIGARD terdiri dari 2 (dua) suntikan. Satu suntikan mengandung zat aktif dalam bentuk serbuk. Suntikan yang lain digunakan untuk melarutkan serbuk. Isi dari kedua suntikan ini dicampur sesaat sebelum digunakan.

ELIGARD 7.5mg (1 bulan): Injeksi 1 (satu) kali tiap 1 (satu) bulan
ELIGARD 22.5mg (3 bulan): Injeksi 1 (satu) kali tiap 3 (tiga) bulan
ELIGARD 45mg (6 bulan): Injeksi 1 (satu) kali tiap 6 (enam) bulan

ELIGARD bekerja terus menerus dan konsisten di antara waktu injeksi.

## PERINGATAN DAN PERHATIAN

### PERINGATAN DAN PERHATIAN SERIUS
ELIGARD harus diresepkan oleh dokter yang sudah berpengalaman dengan jenis obat seperti ini.

ELIGARD dapat menyebabkan:

- Memburuknya gejala dari kanker prostat di awal pengobatan
- Pengeroposan tulang

ELIGARD tidak boleh digunakan untuk wanita dan anak – anak dibawah 18 tahun.

**Sebelum menggunakan ELIGARD bicarakan dengan dokter atau apoteker anda jika anda:**
- Alergi terhadap *leuproline acetate*.
- Menggunakan obat-obatan lainnya yang diresepkan dokter.
- Mempunyai riwayat gangguan saluran kemih.
- Mengalami kanker yang telah menyebar ke tulang belakang atau mempunyai riwayat kompresi/penekanan tulang belakang.
- Memiliki penyakit anemia.
- Keluarga anda mempunyai riwayat osteoporosis yang berat. ELIGARD dapat meningkatkan risiko osteoporosis dan patah tulang.
- Memiliki penyakit diabetes (kadar gula di dalam darah tinggi)
- Memiliki riwayat penyakit jantung

## EFEK SAMPING YANG DAPAT TERJADI

Efek samping yang biasanya terjadi:
- Rasa terbakar pada wajah
- Warna kemerahan pada kulit
- Rasa kelelahan
- Rasa terbakar pada tempat yang disuntikkan

Efek samping yang dapat terjadi:
- Gangguan tekanan darah
- Mual dan diare
- Berkeringat di malam hari
- Nyeri otot
- Rasa tidak nyaman pada tempat yang disuntikkan

Jika terdapat efek samping, bicarakan dengan dokter atau apoteker anda. Termasuk efek samping yang tidak tercantum di dalam leafet ini.

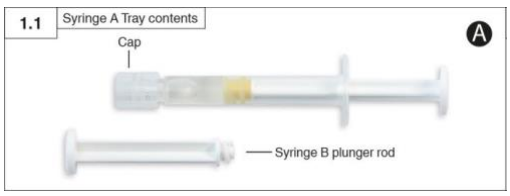
## CARA PENGGUNAAN

Gunakan seperti cara yang tertulis dibawah ini:

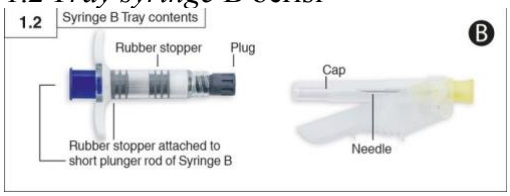
Tempatkan obat pada suhu ruangan dengan memindahkannya dari kulkas sebelum digunakan.

Siapkan pasien terlebih dahulu, diikuti dengan persiapan produk dengan menggunakan instruksi dibawah ini:

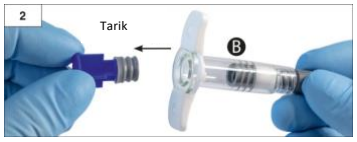
**Langkah 1:**
Buka kedua *tray* (sobek kertas perak dari bagian sudut dilihat dari adanya gelembung kecil) dan pindahkan isi ke dalam tempat lain yang bersih (dua *tray* terdiri dari *Syringe* A (gambar 1.1) dan *Syringe* B (gambar 1.2)). Buang kantong bahan pengering (*desiccant*).
1.1 *Tray syringe* A berisi



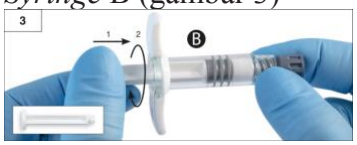
1.2 *Tray syringe* B berisi




**Langkah 2:**
**<u>Tarik keluar</u>** dan **jangan putar** *plunger rod* yang berwarna biru bersama dengan *stopper* berwarna abu-abu dari *Syringe* B lalu buang (gambar 2). **Jangan mencampur obat jika kedua *stopper* masih ada.**



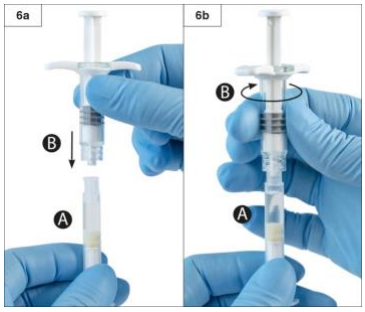

**Langkah 3:**
Putar perlahan *Syringe* B *plunger rod* yang berwarna putih ke *stopper* yang berwarna abu-abu di *Syringe* B (gambar 3)



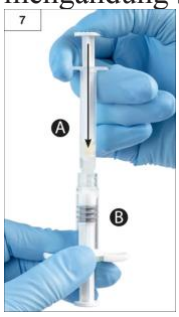

**Langkah 4:**
Tarik tutup karet abu-abu dari *Syringe* B dan letakkan *Syringe* tersebut (gambar 4).


**Langkah 5:**
Tahan *Syringe* A dalam posisi vertikal untuk memastikan tidak ada kebocoran dan buka tutup transparan dari *Syringe* A (gambar 5).

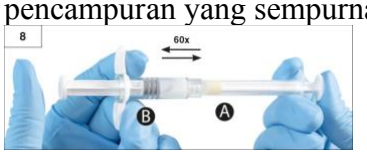

**Langkah 6:**
Gabungkan dua *Syringe* dengan menekan dan memutar *Syringe* B ke *Syringe* A sampai aman (gambar 6a dan 6b). **Jangan terlalu kencang.**



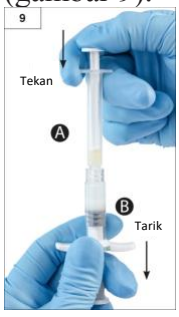

**Langkah 7:**
Balikkan *Syringe* yang telah terhubung dan terus pegang *Syringe* secara vertikal dengan *Syringe* B berada di bagian bawah sementara menyuntikkan isi cairan dari *Syringe* A ke *Syringe* B yang mengandung serbuk (*leuproline acetate*) (gambar 7).




**Langkah 8:**
Campur produk dengan cara mendorong secara lembut isi dari kedua *Syringe* secara bolak-balik (total 60 kali, yang berlangsung sekitar 60 detik) dalam posisi horizontal untuk mendapatkan larutan yang kental homogen (gambar 8). Jangan menekuk *Syringe* (harap diperhatikan bahwa hal ini dapat menyebabkan kebocoran karena anda mungkin membuka sebagian tutup *Syringe*).
**Ketika dicampur, larutan kental akan mempunyai warna sekitar putih sampai dengan kuning pucat (termasuk warna putih sampai kuning pucat).**
**Penting: setelah proses pencampuran segera lanjutkan ke langkah berikutnya karena larutan akan menjadi lebih kental dari waktu ke waktu. Jangan masukkan larutan produk ke dalam lemari pendingin.**
Catatan: produk harus dicampur seperti instruksi; pengocokan TIDAK AKAN memberikan pencampuran yang sempurna.

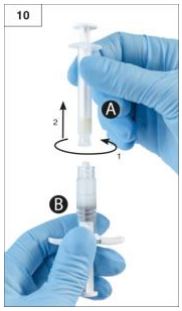



**Step 9:**
Pegang *syringe* secara vertikal dengan *Syringe* B berada di bagian bawah. Kedua *syringe* harus dalam keadaan yang aman. Pindahkan semua larutan produk ke *Syringe* B (*Syringe* yang pendek dan lebar) dengan cara: menekan *plunger Syringe* A ke bawah dan sedikit menarik *plunger Syringe* B (gambar 9).




**Langkah 10:**
Putar dan lepaskan *Syringe* A sambil terus menekan kebawah pada *plunger Syringe* A (gambar 10).

Pastikan tidak ada kebocoran pada produk yang mengakibatkan ketidakamanan ketika produk terpasang dengan jarum.
Catatan: mungkin akan terdapat satu gelembung besar atau beberapa gelembung kecil – hal ini dapat diterima.
**Jangan menghilangkan gelembung tersebut dari *Syringe* B pada tahap ini atau produk akan rusak!**




**Langkah 11:**

- Tahan *Syringe* B dengan tegak dan tahan pada bagian plunger putih untuk mencegah kebocoran produk.
- Buka kemasan jarum dengan membuka kertas pembungkus dan keluarkan jarum dengan hati-hati. Jangan melepaskan pelindung jarum yang terpasang.
- Pasang jarum ke *Syringe* B dengan memegang *syringe* dan memutarnya searah dengan jarum jam (gambar 11).

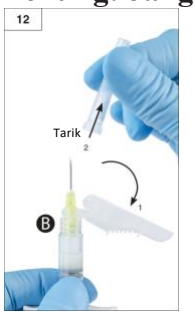
**Jangan terlalu kencang** karena mungkin dapat menyebabkan keretakan pada hub jarum yang menyebabkan kebocoran produk selama diinjeksikan
Apabila hub jarum retak, terlihat rusak, atau bocor, produk tidak dapat digunakan. Jarum yang rusak tidak dapat disubstitusi/digantikan dan produk tidak dapat diinjeksikan. Keseluruhan produk harus dimusnahkan secara aman.

Jika terjadi kerusakan pada hub jarum, penggantian produk baru harus dilakukan.

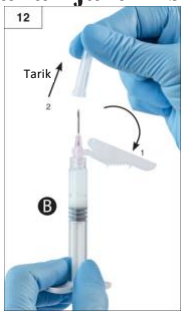
Eligard 7.5 mg/22.5 mg

Eligard 45 mg

**Langkah 12:**
Lepaskan pelindung jarum dan tarik ke atas tutup jarum sebelum penggunaan (gambar 12).
**Penting: Jangan gunakan jarum sebelum akan digunakan ke pasien.**



Eligard 7.5 mg/22.5 mg



Eligard 45 mg

**Langkah 13:**
Sebelum penggunaan, hilangkan gelembung udara yang besar dari *Syringe* B. Berikan produk secara subkutan dan jaga jarak antara pelindung dengan jarum. Pastikan semua larutan dalam *Syringe* B telah disuntikkan.

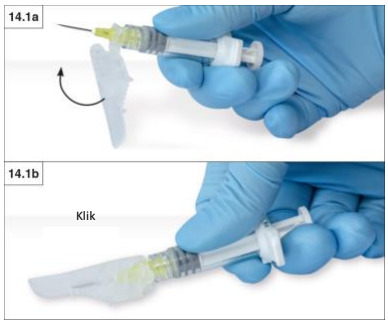
**Langkah 14:**
Setelah penyuntikan, kunci pelindung dengan metode dibawah:

1. **Penutupan pada permukaan datar**

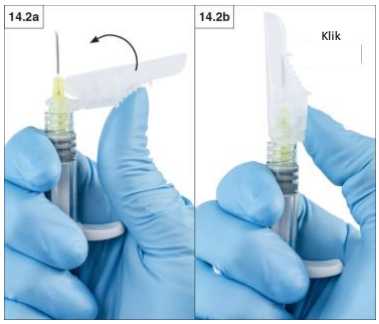
Tekan pelindung, pada tuas sisi, ke permukaan datar (gambar 14.1a dan b) untuk menutupi jarum dan mengunci pelindung.
Verifikasi posisi mengunci dengan terdengarnya bunyi "klik". Posisi terkunci benar-benar akan menutupi ujung jarum (gambar 14.1b).

2. **Penutupan menggunakan ibu jari**

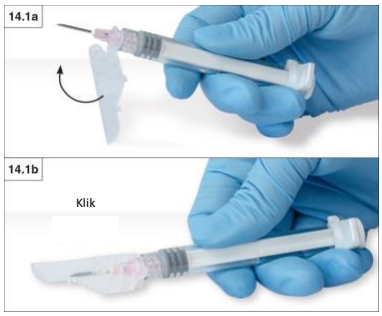
Tempatkan ibu jari pada tuas sisi(gambar 14.2a dan b),menutupi jarum dan mengunci pelindung.
Verifikasi posisi mengunci dengan terdengarnya bunyi "klik". Posisi terkunci benar-benar akan menutupi ujung jarum (gambar 14.ab)



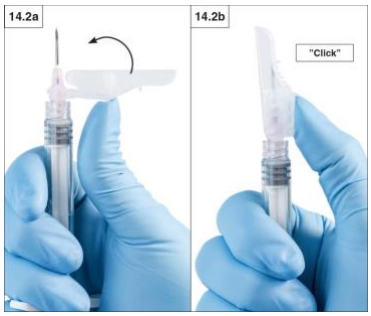
Eligard 7.5 mg/22.5 mg



Eligard 7.5 mg/22.5 mg



Eligard 45 mg



Eligard 45 mg

**Langkah 15:**
Setelah pelindung terkunci, segera buang jarum dan *syringe* dalam wadah yang sesuai.

**CARA PENYIMPANAN**
Simpanlah di dalam kulkas atau suhu dingin (2°C - 8°C) dalam kemasan aslinya untuk melindungi dari kelembaban. Produk ini harus disimpan dalam suhu ruangan sebelum disuntikkan. Pindahkan dari kulkas sebelum digunakan.

**PEMEGANG IJIN EDAR, PRODUSEN DAN PENGEMAS**
Pemegang Ijin Edar
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