Abbreviated prescribing information

Abbreviated Prescribing Information Eligard® Powder and Solvent for Solution for Injection, containing leuprorelin acetate. **INDICATIONS:** For the palliative treatment of hormone dependent advanced prostate cancer. **POSOLOGY AND METHOD OF ADMINISTRATION:** **Posology** Adult Males ***ELIGARD*** is administered as a single subcutaneous injection every month for 7.5mg, every three months for 22.5 mg and every six months for 45 mg. The injected solution forms a solid medicinal product delivery depot and provides continuous release of leuprorelin acetate. 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. As lack of efficacy may result from incorrect preparation, reconstitution, or administration, testosterone levels should be evaluated in cases of suspected or known handling errors. **Method of Administration** ELIGARD should be prepared, reconstituted and administered only by healthcare professionals who are familiar with these procedures. If the product is not prepared appropriately, it should not be administered. The contents of the two pre-filled sterile syringes must be mixed immediately prior to administration by subcutaneous injection. Based on data from animal experience, intra-arterial or intravenous injection has to be strictly avoided. The injection site should be varied periodically. The specific injection location chosen should be an area with sufficient soft or loose subcutaneous tissue that does not have excessive pigment, nodules, lesions, or hair. Avoid areas with brawny or fibrous subcutaneous tissue or locations that could be rubbed or compressed (e.g. with a belt or clothing waistband). **CONTRAINDICATIONS:** ELIGARD is contraindicated in women and in paediatric patients. 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. **SPECIAL WARNINGS AND SPECIAL PRECAUTIONS FOR USE: Correct reconstitution:** Cases of handling errors which can occur during any step of the preparation process, and which could potentially result in lack of efficacy have been reported. Instructions for reconstitution and administration must be strictly followed. In cases of suspected or known handling error, patients should be monitored appropriately. **Androgen deprivation therapy may prolong the QT interval:** In patients with a history of or risk factors for QT prolongation and in patients receiving concomitant medicinal products that might prolong the QT interval, physicians should assess the benefit risk ratio including the potential for Torsade de pointes prior to initiating ELIGARD. Electrolyte abnormalities should be corrected. Consider periodic monitoring of electrocardiograms and electrolyte. **Cardiovascular diseases:** Increased risk of developing myocardial infarction, sudden cardiac death and stroke has been reported in association with the 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 GnRH agonists should be monitored for symptoms and signs suggestive of development of cardiovascular disease and be managed according to current clinical practice. **Transient testosterone flare:** 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. 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. **Bone density:** Decreased bone density has been reported in the medical literature in men who have had orchiectomy or who have been treated with GnRH agonists. 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. **Pituitary apoplexy:** 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. **Hyperglycemia and diabetes:** Hyperglycemia and an increased risk of developing diabetes have been reported in men receiving GnRH agonists. 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. **Convulsions:** 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. **Other events:** 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. **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. Tabulated list of adverse reactions: 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
Cardiac disorders	
not known	QT prolongation
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, rigors, weakness
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
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, anemia
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, 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. 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 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 analogue. 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 (refer Package Insert). ***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.

Full prescribing information is available on request.

Reference: Eligard® Package Insert, Singapore.

Report any adverse events to DCH Auriga Singapore Pte. Ltd. at SGPDrugSafety@dchauriga.com. Alternatively, adverse events may be reported to the Health Sciences Authority at https://www.hsa.gov.sg/adverse-events or email to HSA_productsafety@hsa.gov.sg

This document has been approved by HSA on 01-04-2022 DCHA-1021-064

Marketed & Distributed by,

DCH AURIGA
Asia Healthcare Solutions
10 Raeburn Park, Blk C, 01-33, S(088702)

Eligard®
(leuprolide acetate) for injectable suspension

Eligard® (leuprorelin acetate): Instructions for preparation

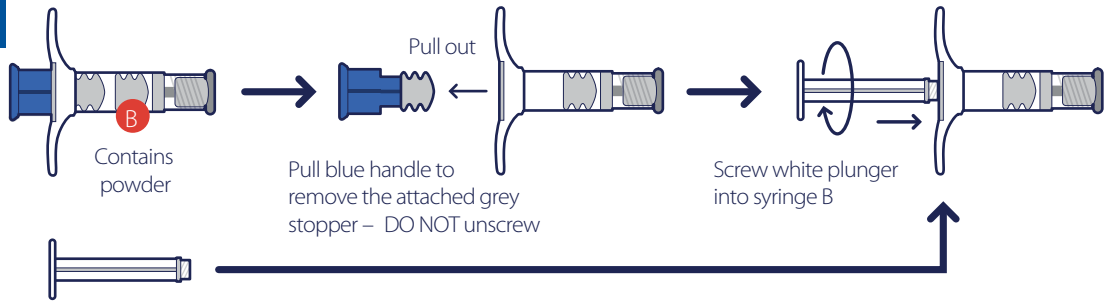
DCH AURIGA
Asia Healthcare Solutions

Eligard®
(leuprolide acetate) for injectable suspension

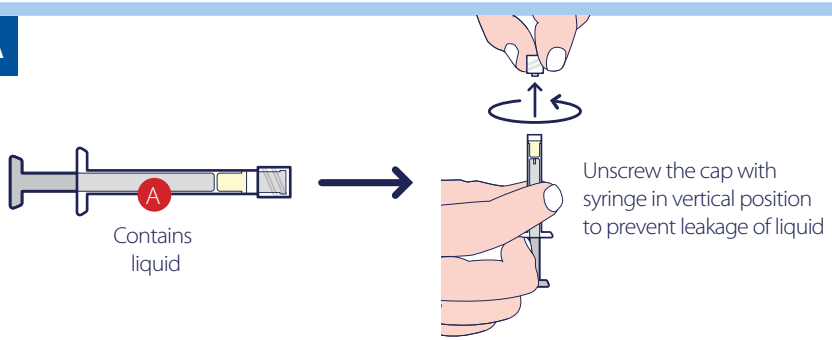
Eligard®
(leuprolide acetate) for injectable suspension

Instructions for preparation

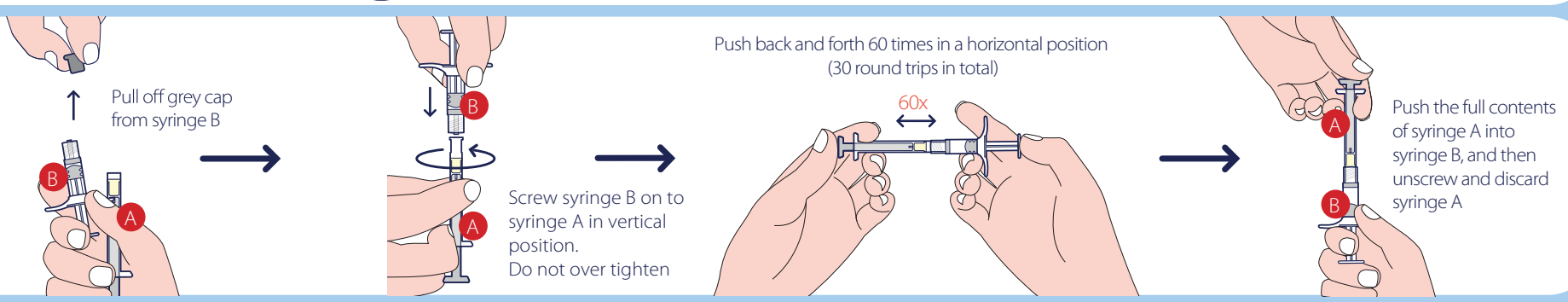
STEP 1 Syringe B



STEP 2 Syringe A

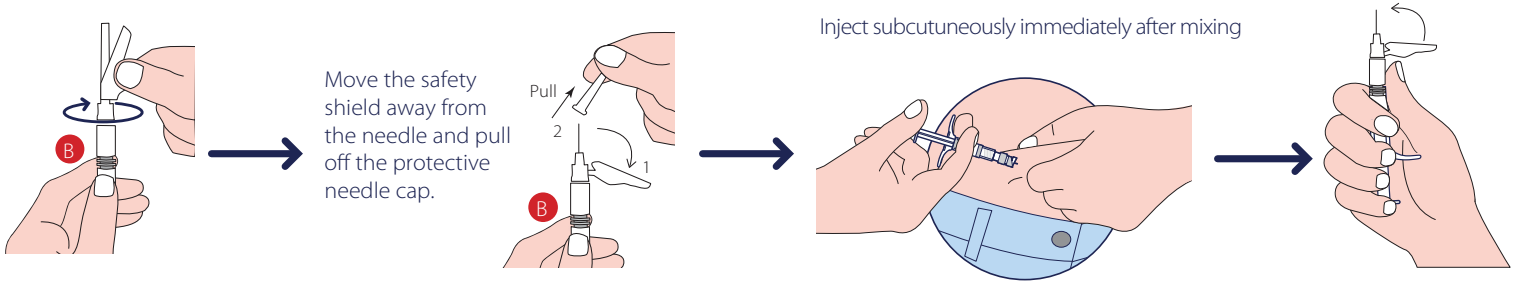


STEP 3 Mixing



STEP 4 Administration

Attach the safety needle to Syringe B by turning the needle clockwise with approximately a three-quarter turn until the needle is secure. Do not over tighten.



IMPORTANT INFORMATION FOR ELIGARD PREPARATION

Please read before mixing

Before mixing Eligard, familiarise yourself with, and then carefully follow, the instructions in the package leaflet.

- Store in the refrigerator (2–8°C) in the original package
- Always allow Eligard to reach room temperature before mixing (remove from fridge 30 minutes prior to reconstitution)
- Prepare the patient for the injection first, and subsequently prepare the product
- Administer Eligard subcutaneously immediately after reconstitution
- Eligard should only be prepared and administered by a healthcare professional
- If the product is not prepared using the proper technique, the product should not be administered to any patient

REPORTING ADVERSE EVENTS

- All cases of incorrect storage, preparation, reconstitution, and administration of Eligard or any other adverse events should be reported to:

Health Sciences Authority of Singapore
Email: HSA_productsafety@hsa.gov.sg
Online: https://www.hsa.gov.sg/adverse-events

And

DCH Auriga Singapore
Email: SGPDrugSafety@dchauriga.com
Fax: (65) 6861 7372

Abbreviated prescribing information can be found on the reverse