Leuprolide Acetate for Injection 11.25 mg (Depot) LUPRODEX

INDICATIONS AND USAGE: in the initial days of therapy, but these will dissipate with potential risk to the fetus. discontinued and the patient must be apprised of the risk to the fetus. Therefore, patients should use non-hormonal insurance, however, by taking breakdown and renal excretion. Metabolism: it is metabolized into its metabolites in provides plasma concentrations of Leuprolide over a period of three months, underwent bone density studies as a result of therapy, retreatment with a six months course of Leuprolide Acetate results in suppression or "down-regulation" of gonadotropins, chronic stimulation with Leuprolide may cause female harm when administered to a pregnant woman. Use Aseptic Precautions throughout. opioid growth factor receptors in the prostate, breast, and other tissues. (3 months Depot) LUPRODEX (DEPOT) 11.25 mg: Each vial contains: Leuprolide B.P. (As acetate) ....... 11.25 mg Excipients : Polylactic acid, Mannitol I.P. For Intramuscular / Subcutaneous use For Single use only Not for Intravenous Administration

CONTRAINDICATIONS: Leuprolide Acetate is a synthetic nonapeptide analog of naturally occurring gonadotropin-releasing hormone (GnRH or LH-RH). The analog possesses greater potency than the natural hormone. LUPRODEX (DEPOT) 11.25 mg is contraindicated in women who are pregnant while receiving the drug. LUPRODEX (DEPOT) 11.25 mg may cause fetal harm when administered to a pregnant woman. 1. Hypersensitivity to GnRH, GnRH agonist analogs or leuprolide. 2. Undiagnosed abnormal vaginal bleeding. 3. LUPRODEX (DEPOT) 11.25 mg is contraindicated in men who have had orchidectomy or who have been treated with an LH-RH agonist analog. In a clinical trial, 25 men with prostate cancer, 12 of whom had been treated previously with leuprolide acetate for at least six months, underwent bone density studies as a result of therapy. This may occur due to increased testosterone level during the first week of treatment. Concurrent administration of an androgen antagonist like flutamide prevents the flare phenomenon in male patients. LUPRODEX (DEPOT) 11.25 mg three monthly and LUPRODEX (DEPOT) 11.25 mg alone. LUPRODEX (DEPOT) 11.25 mg must be administered under the supervision of a physician. Intramuscular injection of the depot formulation provides plasma concentrations of Leuprolide over a period of three months. Distribution: Distributed to kidney, liver, spleen and lymph nodes. Metabolism: It is metabolized into its metabolites in hypothalamus and anterior pituitary gland. Elimination: Leuprolide is eliminated by enzymatic breakdown and renal excretion. When used three monthly at the recommended dose, LUPRODEX (DEPOT) 11.25 mg usually inhibits ovulation and stops menstruation. Contraception is not ensured, however, by taking LUPRODEX (DEPOT) 11.25 mg. Therefore, patients should use non-hormonal methods of contraception. Patients should be advised to see their physician if they believe they may be pregnant. If a patient becomes pregnant during treatment, the drug must be discontinued and the patient must be apprised of the potential risk to the fetus. During the early phase of therapy, sex steroids temporarily rise above baseline because of the physiologic effect of the drug. Therefore, an increase in clinical signs and symptoms may be observed during the initial days of therapy, but these will dissipate with continuing therapy.

Endometriosis: LUPRODEX (DEPOT) 11.25 mg is indicated in the treatment of endometriosis, including pain relief and reduction of endometriotic lesions. Duration of initial treatment or retreatment should be limited to 6 months. LUPRODEX (DEPOT) 11.25 mg can be used as sole therapy when it may provide symptomatic relief for women who do not desire surgery as an adjunct to surgery. Uterine Leiomyomata (Fibroids): LUPRODEX (DEPOT) 11.25 mg concomitantly with iron therapy is indicated for the preoperative hematologic improvement of patients with anemia caused by uterine leiomyomata. LUPRODEX (DEPOT) 11.25 mg may be added if the response to iron is considered inadequate. Recommended duration of therapy with LUPRODEX (DEPOT) 11.25 mg is up to six months.

Advanced Prostate Cancer (Palliative Treatment): LUPRODEX (DEPOT) 11.25 mg is indicated in the treatment of advanced prostatic cancer. It offers an alternative treatment of prostatic cancer when chemotherapy or estrogen administration are either not indicated or unacceptable to the patient. SIDE EFFECTS & ADVERSE REACTIONS: Flare phenomenon is the commonly occurring side effect of Leuprolide (symptoms of hot flushes, sweats, peripheral oedema, GI upset). Temporary increase in the degree of bone pain and obstructive voiding symptoms have been noted within the first 72 hours of therapy. This may occur due to increased testosterone level during the first week of treatment. Concurrent administration of an androgen antagonist like flutamide prevents the flare phenomenon in male patients. Long term usage leading to decreased bone density has been reported in the medical literature in men who have had orchidectomy or who have been treated with an LH-RH agonist analog. In a clinical trial, 25 men with prostate cancer, 12 of whom had been treated previously with leuprolide acetate for at least six months, underwent bone density studies as a result of therapy. The leuprolide-treated group had lower bone density scores than the non-treated control group. It can be anticipated that long periods of medical treatment in men will have effects on bone density. Anaphylactic or anaphylactoid reaction have been rarely reported. Flush, urticaria, and photosensitivity reactions have also been reported. Also a localized reaction including induration and abscess at the site of injection.

Other reactions reported are: Cardiac System - Myocardial infarction, increased blood pressure, congestive heart failure, atrial fibrillation, angina; Respiratory System - Respiratory distress, shortness of breath; Gastrointestinal System - Nausea, vomiting, diarrhea, flatulence, abdominal discomfort, constipation, increased appetite, weight gain, enlargement of liver; Gastrointestinal - Diarrhea, dry mouth, steatorrhea, nausea, vomiting, abdominal pain; Genitourinary System - Female genital swelling, vaginitis; Male genital system - Testicular pain, gynecomastia; Endocrine System - Change in libido, gynecoid body habitus; Blood & Lymphatic System - Decreased WBC, anemia; Other: Flu, chills, asthenia, arthralgia, headache, menorrhagia, tissue edema, weight gain, deep vein thrombosis, pulmonary embolism; Drug / Laboratory Test Interactions:

- Cardiovascular System - Hypotension, Pulmonary edema, tachycardia, congestive heart failure
- Gastrointestinal System - Steatorrhoea, nausea, vomiting, diarrhea, constipation, abdominal pain, flatulence, weight gain
- Genitourinary System - Male genital system changes, pain, gynecomastia, female genital swelling, vaginitis
- Endocrine System - Change in libido, gynecoid body habitus
- Blood & Lymphatic System - Decreased WBC, anemia
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LUPRODEX (DEPOT) 11.25 mg must be administered under the supervision of a physician.

Endometriosis: The recommended duration of treatment with LUPRODEX (DEPOT) 11.25 mg alone or in combination with nonsteroidal acetate is six months. The choice of LUPRODEX (DEPOT) 11.25 mg alone or LUPRODEX (DEPOT) 11.25 mg plus nonsteroidal acetate therapy for initial management of the symptoms and signs of endometriosis should be made by the health care professional in consultation with the patient and should take into consideration the risks and benefits of the addition of nonsteroidal to LUPRODEX (DEPOT) 11.25 mg alone. If the symptoms of endometriosis recur after a course of therapy, retreatment with a six months course of LUPRODEX (DEPOT) 11.25 mg three monthly and nonsteroidal acetate 5 mg daily may be considered.

Drug / Laboratory Test Interactions:

- Cardiovascular System - Hypotension, Pulmonary edema, tachycardia, congestive heart failure
- Gastrointestinal System - Steatorrhoea, nausea, vomiting, diarrhea, constipation, abdominal pain, flatulence, weight gain
- Genitourinary System - Male genital system changes, pain, gynecomastia, female genital swelling, vaginitis
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1. Ensure that the diluent fluid is at the bottom section of the ampoule of diluent. Open the ampoule from the tip.
2. Using a syringe with 22 gauge needle, withdraw 1.5 ml of diluent from the ampoule. (Extra diluent is provided; any remaining unused portion should be discarded).
3. Remove the plastic seal cap from the vial.
4. Inject the diluent from the syringe into the glass vial.
5. Shake well for thorough dispersion of particles to obtain a uniform suspension. (The suspension will appear milky).
6. Withdraw entire contents from the vial into the syringe.
7. Inject intramuscularly / subcutaneously.
8. Discard the unused product remaining in the vial along with the unused diluent remaining in the ampoule.

The product has been shown to be stable for 24 hours following reconstitution. Since the product does not contain a preservative, the reconstituted product should be discarded if not used immediately.

**OVERDOSAGE:**
In rats subcutaneous administration of 250 to 500 times the recommended human dose, expressed on a per body weight basis, resulted in dyspnea, decreased activity, and local irritation at the injection site. There is no evidence that there is a clinical counterpart of this phenomenon. In early clinical trials using daily subcutaneous Leuprolide Acetate in patients with prostate cancer, doses as high as 20 mg/day for up to two years caused no adverse effects differing from those observed with the 1 mg/day dose.

**STORAGE:**
Store below 25 C. Do not freeze.

**PRESENTATION:**
Each pack of LUPRODEX (DEPOT) 11.25 mg is supplied as one vial containing microspheres equivalent to 11.25 mg of Leuprolide Acetate along with one ampoule of diluent for reconstitution, one disposable syringe, two needles and two alcohol swabs.

**REFERENCES:**


Procedure for Reconstitution:

**LUPRODEX® (DEPOT) 11.25 mg**

**Use Aseptic Technique Throughout**

Do not use Sterile Water for Injection or Sodium Chloride Injection (Saline) for reconstitution in place of the recommended diluent provided with this pack.

**Use luer lock syringe with 22 gauge needle provided with this pack.**

Fix needle in luer lock till it rotates no more.

Withdraw 1.5 ml of diluent from the ampoule.

Remove plastic seal cap of vial by flicking it off.

Inject diluent into the vial.

Shake well the contents of vial for thorough Dispersion.

The suspension will appear uniformly milky.

Withdraw entire contents of the vial back in the syringe.

Inject intramuscularly / subcutaneously

Discard the remainder of the diluent, the ampoule and the vial.

In case of suspected Adverse Reactions, contact Bharat Serum and Vaccines at pab@bharatserum.com or visit the website www.bharatserum.com/adverse.html

Manufactured in India by:
BHARAT SERUMS AND VACCINES LIMITED
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Ambernath (E) - 421 501

Use Aseptic Technique Throughout.