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

The medicine is dispensed with a doctor's prescription only

Lucrin® PDS Depot 3.75 mg
leuprorelin acetate 3.75 mg
Powder and solvent for suspension for injection

Lucrin® PDS Depot 11.25 mg
leuprorelin acetate 11.25 mg
Powder and solvent for suspension for injection

Inactive ingredients and allergens in the medicine – see section 6 "Further Information".

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.
This medicine has been prescribed to treat your ailment. Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?
Lucrin PDS Depot is intended to treat:
- Endometriosis (migration of uterine mucosal tissue to outside of the uterus) for a period of up to six months
- Uterine fibroids (myomas) for a period of up to six months
- Prostate cancer for a period of up to six months
- Breast cancer in premenopausal and postmenopausal women who require hormonal treatment

Lucrin PDS Depot 11.25 mg is suitable for patients requiring hormonal treatment for a period of at least three months.
This medicine is not usually intended for infants and for children under 18 years of age.

Therapeutic group: Inhibitor of gonadotropin secretion when given on a continuous basis.
Leuprorelin is a synthetic nonapeptide analogue of the endogenous hormone Gonadotropin Releasing Hormone (GnRH; also known as LHRH). Its mechanism of action upon continuous administration is inhibition of secretion of the gonadotropins, resulting in suppression of secretion of sex hormones from the ovaries and testes.
Upon use of leuprorelin, LH, FSH and sex hormone levels drop.

2. BEFORE USING THE MEDICINE
Do not use the medicine:
- if you are sensitive (allergic) to the active ingredient (synthetic GnRH), to similar nonapeptides or to any of the other ingredients contained in the medicine (for the list of inactive ingredients, see section 6 "Further Information").
- during pregnancy, or if you can become pregnant during the course of treatment.
- when breastfeeding.
- if you are suffering from abnormal vaginal bleeding, which was neither reported to nor discussed with the attending doctor.
- after surgery for removal of the testicles.

Special warnings regarding use of the medicine:
- Use Lucrin PDS Depot under medical supervision.
- At the beginning of treatment with the medicine, the clinical symptoms may temporarily worsen, but these symptoms usually disappear with continued treatment. Worsening of the symptoms may cause paralysis, with or without complications that can lead to death.
- Although use of Lucrin PDS Depot causes cessation of menstruation, this medicine is not itself a contraceptive. Use a non-hormonal contraceptive during the course of treatment with Lucrin PDS Depot. If you are uncertain about this issue, consult the attending doctor.

Before treatment with Lucrin PDS Depot, tell the doctor if you are suffering, or have suffered in the past, from:
- Diabetes - check blood sugar levels regularly. Among men, cases of increased blood sugar levels and risk of developing diabetes have been reported. Therefore, blood glucose levels and hemoglobin A1C levels should be monitored.
- Depression - consult the doctor regularly since Lucrin PDS Depot may aggravate preexisting depression.
- Changes in bone density among men (upon prolonged use of the medicine) and in women may occur. There are no data regarding the reversibility of loss of bone density among men after discontinuing treatment with the medicine.
  In women, reduced bone density can be reversible after discontinuation of the treatment with the medicine.
  Therefore, tell the doctor if you or a family member suffer(s) from osteoporosis.
- If you consume large amounts of alcohol.
- Cases of convulsions (seizures) in patients treated with Lucrin PDS Depot have been reported. These incidents have been observed in women and children, in patients with a history of seizures, epilepsy, cerebrovascular disturbances, central nervous system anomalies or tumors, and in patients on concomitant medications that have been associated with convulsions, such as: bupropion and SSRI antidepressants. Convulsions have also been reported in patients without any of the above-mentioned conditions. Tell the doctor if any of the above-mentioned conditions applies to you.
- If you took steroids, e.g., hydrocortisone or prednisolone, for a long period of time.

In women:
- If menstruation continues after initiating treatment with Lucrin PDS Depot.
- Cases of heavy vaginal bleeding requiring medical or surgical intervention have been reported in women with uterine fibroids. In case of severe unusual bleeding or pain, refer to the doctor immediately!

In men:
- In male patients, there is an increased risk of developing myocardial infarction, sudden cardiac death and stroke when using GnRH agonists, although the risk is low. Therefore, the cardiovascular risk and risk factors should be evaluated in prostate cancer patients. Patients receiving GnRH agonists must be monitored for symptoms and signs suggestive of development of cardiovascular disease. Tell the doctor if you are suffering from a heart condition, if you have had in the past a heart attack, stroke, or cardiovascular risk factors, such as: high blood pressure, high cholesterol or smoking.
  Tell the doctor if you suffer, or have suffered in the past, from arrhythmias, abnormal blood electrolyte levels, heart failure or are taking medicines to treat arrhythmias (such as: quinidine, disopyramide, amiodarone, sotalol, dofetilide, ibutilide), methadone, moxifloxacin, antipsychotics.
  Since treatment with Lucrin may prolong the QT interval, the doctor must carefully assess the treatment with this medicine in relation to the other medicines you are taking.
- During the first few weeks of treatment, patients with prostate cancer may experience temporary exacerbation of existing symptoms or additional symptoms and signs of prostate cancer. A small number of patients experience a temporary increase in bone pain. In addition, isolated incidents of obstruction of the urethra or pressure on the spinal cord, which may lead to paralysis with or without complications that can lead to death, have been reported. Therefore, tell the doctor if you are suffering from a urinary tract obstruction, bloody urine or from pressure on the spinal cord.
- If you have metastases in the spinal vertebrae.
- If you have been treated in the past with synthetic hormone injections that were not beneficial.
- If you underwent surgery for removal of the testicles.

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

Pregnancy and breastfeeding
- Do not use if you are pregnant or may become pregnant during the course of treatment.
- Do not use if you are breastfeeding.

Use of the medicine and consumption of alcohol
- Do not drink large quantities of wines or alcoholic beverages during the course of treatment with the medicine.

Driving and use of machinery
- Use of this medicine may cause dizziness and vision disturbances and therefore requires that caution be exercised when driving a car, operating machinery and when engaging in any activity that requires alertness.

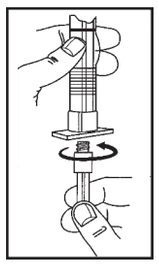
3. HOW SHOULD YOU USE THE MEDICINE?
Always use according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain.
The dosage and treatment regimen will be determined by the doctor only. **Do not exceed the recommended dose.**

Lucrin PDS Depot is administered by intramuscular or subcutaneous injection.
Use this medicine at set intervals, as determined by the attending doctor.
If it seems to you that the medicine is having an effect that is too strong or too weak, consult the attending doctor.

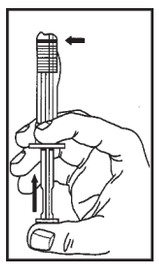
Directions for use:
Use the medicine under medical supervision. Use the suspension immediately after its reconstitution and discard any remainder.
The injection site must be changed periodically.

Instructions for mixing and injecting:
Lucrin PDS Depot is a sterile aqueous solution provided in a pre-filled dual-chamber syringe.
One chamber has microspheres which contain the active ingredient, and the other chamber contains the diluent.
An injectable suspension is obtained upon mixture of the contents of both chambers.
A medical staff member will follow the instructions below to prepare the medicine for injection.

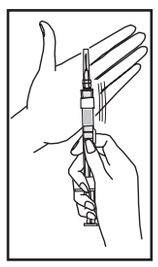
1. To prepare the injection, screw the white plunger into the stopper at the end of the syringe, until the stopper begins to turn around itself.
   Important: Do not pull the plunger out throughout the entire procedure detailed below.



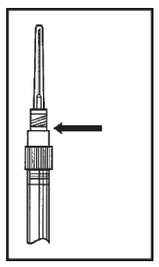
2. Hold the syringe with its needle pointing upward, and release the diluent into the powder by slowly pushing (for 6 to 8 seconds) the plunger. Push the plunger until the first stopper is opposite the blue line in the middle of the barrel.
   Important: Pushing the plunger too fast or beyond the blue line may result in leakage of the suspension through the needle.



3. Hold the syringe with its needle pointing upward, and gently tap the syringe on the palm of your hand to thoroughly mix the particles of the medicine until a uniform suspension is obtained. The obtained suspension will appear milky.
   Important: Avoid tapping firmly, to prevent formation of air bubbles.



4. Hold the syringe with its needle pointing upwards, and remove the needle cap with the opposite hand by pulling it upward. Gently push the plunger upward to expel the air bubbles from the syringe.
   Important: When removing the needle cap, avoid twisting, so that the connection between the needle and the syringe will not come loose.



5. Inject the entire contents of the syringe intramuscularly or subcutaneously, as you would with any other injection.
   Important: Use the medicine immediately after its reconstitution. The suspension settles very quickly following reconstitution; therefore, prepare the suspension and inject it immediately thereafter.
   Note: If you accidentally penetrated a blood vessel during the injection, you will see blood being pulled up below the connection between the needle and syringe. Blood will also be visible at the needle hub.

Tests and follow-up
- During the course of treatment with this medicine, the following tests should be performed: sex hormone and PSA levels.
- Sometimes, bone density must be checked before commencement of treatment with Lucrin PDS Depot.
- Lucrin PDS Depot may cause a change in blood sugar levels.
  Therefore, you should monitor blood glucose levels and check hemoglobin A1C levels.
  Blood sugar levels should be monitored more often in diabetes patients being treated with this medicine.
- Monitor for signs and symptoms suggestive of development of cardiovascular disease.
- During the first few weeks of treatment, the attending doctor will closely monitor patients with metastases in the vertebrae or obstruction of the urinary tract .

If you accidentally take too high a dosage
If you suspect that you injected too high a dose of Lucrin PDS Depot, refer to the attending doctor immediately! You must be under close supervision of the doctor. If you took an overdose, or if a child accidentally took the medicine, immediately refer to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forget to take the medicine, refer to the doctor immediately!
Women – if the injection was not given at the designated time, bleeding or ovulation with potential for fertilization may occur. If you suspect pregnancy – stop treatment with Lucrin PDS Depot and refer to the attending doctor immediately!
Do not take a double dose. Adhere to the treatment regimen recommended by the doctor.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them.

If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS
As with any medicine, use of Lucrin PDS Depot may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Refer to the doctor immediately
- if you notice any of the following signs:
  - severe rash
  - itching
  - shortness of breath
  - difficulty breathing

  These effects may be indicative of a severe allergic reaction.
- In the event of severe unusual bleeding or pain, as Lucrin PDS Depot may cause vaginal bleeding.

Refer to the doctor if you notice any of the following signs:
- severe headache that does not improve after taking analgesics
- vision disturbances
- changes in blood pressure
- pounding heartbeat
- changes in blood lipid levels (cholesterol)
- changes in values indicating liver function
- changes in the number of red or white blood cells
- changes in blood sugar levels
- changes in levels of enzymes, electrolytes, iron and acids in the blood
- blood in the stool
- blood in the urine
- severe weight loss
- tumors
- changes in bone density
- decreased testicular size
- impotence
- edema
- unexplained bleeding or bruising
- if you feel generally unwell
- **Men with prostate cancer:** obstruction of the urinary tract and/or pressure on the spinal cord
- **Men with prostate cancer:** worsening of pain, numbness in the legs or difficulty passing urine
  At the beginning of treatment with Lucrin PDS Depot, there may be a rise in testosterone levels, which, in some patients, may result in a temporary increase in local pain and in increased difficulty in passing urine
- **Women:** if menstruation continues after initiating treatment with Lucrin PDS Depot
- **Patients suffering from depression:** Lucrin PDS Depot may worsen it

Additional side effects
Very common – effects that occur in more than one in ten users:
- dilation of blood vessels
- flushing
- increased appetite
- affect lability
- mood swings
- nervousness/anxiety
- decreased libido
- sexual dysfunction
- testicular impairments
- insomnia
- depression
- dizziness
- headache
- hot flushes
- nausea
- acne
- excessive sweating
- joint pain
- back pain
- vulvovaginitis
- weakness
- induration at the site of injection
- feeling hot
- general decline in physical ability
- weight gain or loss
- bone pain
- increased nocturnal urination
- tiredness
- injection site reaction
- pain at the injection site
- increased blood lactic dehydrogenase values

Common – effects that occur in 1-10 out of 100 users:
- tingling sensation
- vomiting
- nausea and vomiting
- retching
- rash
- allergic skin reaction
- injection site mass
- cold
- anxiety
- confusion
- hostility
- sensory change
- ringing in the ears (tinnitus)
- cough
- throat pain
- dry mouth
- inflammation of the mouth
- subcutaneous hemorrhaging
- seborrhea
- dry skin
- mucosal dryness
- bad or abnormal skin odor
- night sweats
- change of pigmentation
- muscle pain
- skeletal muscle stiffness
- menstrual pain
- menstrual disorder
- breast atrophy
- vaginal discharge
- breast pain
- pelvic pain
- menopause effects
- warmth and redness at site of injection
- bronchitis
- urinary tract infection
- anemia
- anorexia
- constipation
- limb pain
- pain when passing urine
- blood in urine
- development of mammary glands, resulting in breast enlargement and secretion of milk
- flu symptoms
- reduced appetite
- sleepiness
- memory decline
- decreased sensitivity
- migraine
- excessive tension
- tremor
- conjunctivitis
- disturbed and blurred vision
- deafness
- sea sickness
- vertigo
- auricular swelling
- nosebleed
- sputum increased
- diarrhea
- abdominal bloating
- flatulence
- gastritis
- gingivitis
- dryness/inflammation of the mouth
- abdominal pain
- skin redness
- balding
- eczema
- excessive hairiness (on the skin)
- joint disease
- joint stiffness
- neck pain
- muscle weakness
- muscle tremor
- changes in frequency of urination
- generalized pain
- chest pain
- fever (pyrexia)
- itching and redness at the injection site
- chills
- feeling thirsty
- agitation
- itching
- major depression
- constipation and vomiting
- breathing difficulties
- asthma
- hypertension
- venous thrombosis
- lymphatic obstruction
- pain
- increased blood alkaline phosphatase values
- increased blood gamma-glutamyltransferase values
- increased blood aspartate aminotransferase values
- increased blood alanine aminotransferase values
- increased blood prostate-specific antigen values
- abnormal ECG
- hypercholesteremia
- blood in the stool
- irregular heartbeat (palpitations)
- sleeping problems
- edema
- peripheral edema
- injection site edema
- development of fatty liver
- impaired liver function
- abdominal distention
- joint damage
- frequent urination
- degenerative joint inflammation
- involuntary muscle contraction and relaxation
- skeletal muscle stiffness
- vaginal bleeding
- reproductive system disorders
- diabetes
- glucose intolerance
- increased blood triglyceride values
- increased blood LDL values
- osteoporosis
- decreased bone density
- flare-up of prostate cancer
- aggravation of prostate cancer
- increased libido
- decreased blood pressure
- orthostatic hypotension
- hypotrichosis (including hair loss, abnormal hair growth)
- testicular atrophy
- anemia (due to iron deficiency)
- inflammation of the nose and throat
- convulsions
- inflammation of the tissues around the joints
- hives (urticaria)
- redness
- abdominal discomfort
- tongue disturbance
- excessive menstrual bleeding
- bleeding at the injection site
- malaise
- breast enlargement
- chest congestion
- swelling of the penis
- penile disturbances
- testicular pain
- cold sweat
- pain in the prostate
- breast tenderness
- nail disorder
- bleeding from the uterus
- painful sexual intercourse
- problems with the uterus

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not listed in the leaflet, consult the doctor.

5. HOW SHOULD THE MEDICINE BE STORED?
- Avoid poisoning! This medicine and any other medicine must be kept in a safe place out of the sight and reach of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.
- Do not store at a temperature that exceeds 25°C.
- Store in the original package, to protect from exposure to light.
- Do not freeze.
- After first opening/reconstitution - use immediately.

6. FURTHER INFORMATION
In addition to the active ingredient, the medicine also contains -

Lucrin® PDS Depot 3.75 mg	**Lucrin® PDS Depot 11.25 mg**
Powder: DL-lactic and glycolic acids copolymer, mannitol and gelatin. Diluent: mannitol, carboxymethylcellulose sodium, polysorbate 80, glacial acetic acid and water for injection.	Powder: Polylactic acid and mannitol. Diluent: mannitol, carboxymethylcellulose sodium, polysorbate 80, glacial acetic acid and water for injection.

- **What the medicine looks like and the contents of the package:**
  The package contains one pre-filled, dual-chamber syringe. One chamber has microspheres which contain the active ingredient, and the other chamber contains the diluent.
- **License holder name and address:** AbbVie Biopharmaceuticals Ltd., 4 Haharash St., Hod Hasharon, Israel.
- **Manufacturer name and address:**
  AbbVie Logistics B.V., Meeuwenlaan 4, 8011 BZ Zwolle, The Netherlands.
- **This leaflet was checked and approved by the Ministry of Health in:**
  May 2015.
- **Registration number of the medicine in the National Drug Registry of the Ministry of Health:**
  Lucrin PDS Depot 3.75 mg: 28779
  Lucrin PDS Depot 11.25 mg: 29491