

Package leaflet: Information for the user

**Leuprorelin 3-month Depot 22.5 mg powder and solvent for prolonged-release
suspension for injection**
leuprorelin acetate

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What **Leuprorelin 3-month Depot** is and what it is used for
2. What you need to know before you use **Leuprorelin 3-month Depot**
3. How to use **Leuprorelin 3-month Depot**
4. Possible side effects
5. How to store **Leuprorelin 3-month Depot**
6. Contents of the pack and other information

1. What **Leuprorelin 3-month Depot is and what it is used for**

Leuprorelin 3-month Depot is a vial containing a white powder, which is made into a suspension for injection into a muscle. **Leuprorelin 3-month Depot** contains the active ingredient leuprorelin (also called **leuprolide**), which belongs to a group of medicines called luteinizing hormone releasing hormone (LHRH) agonists (medicines that reduce testosterone – a sex hormone).

Your doctor has prescribed **Leuprorelin 3-month Depot** for palliative treatment of advanced prostate cancer.

2. What you need to know before you use **Leuprorelin 3-month Depot**

Do not use **Leuprorelin 3-month Depot**:

- if you are allergic (hypersensitive) to LHRH, LHRH agonists or any of the other ingredients of this medicine (listed in section 6). An allergic reaction may include rash, itching, difficulty of breathing or swelling of the face, lips, throat or tongue.
- if you have had an orchiectomy (removal of the testicles).
- if you are female or a child.
- **Leuprorelin 3-month Depot** must not be used alone for the treatment of prostate cancer when the spinal cord is compressed or the cancer has spread to the spine.

Warnings and precautions

- Talk to your doctor or pharmacist before you are given **Leuprorelin 3-month Depot**
- Your condition may get worse at first during the first weeks of the treatment, but should improve with continued treatment. Such signs and symptoms include: temporary increase of testosterone (a male hormone), hot flushes, bone pain, nervous system disorders (including depression) or urinary obstruction.
- If you feel you have experienced an allergic reaction (shortness of breath, asthma, rhinitis, swelling of the face, urticaria, skin eruption), stop using this medicine and inform your doctor.
- Tell your doctor if you might be at risk or if you have any of the following as you may need more frequent check ups:
 - you suffer from any unexplained bruising or bleeding or if you feel generally unwell. Although rare, these could be symptoms of changes in the number of red or white cells
 - you have metabolic disease
 - you have heart problems, or a pounding heart beat
 - you have diabetes
- Your doctor should be aware of any previous personal clinical history of pituitary adenoma (non-cancerous tumor of pituitary). Cases of pituitary apoplexy (partial tissue loss of pituitary gland) have been described after initial administration of this type of drug to patients with pituitary adenoma. Pituitary apoplexy may be manifested by sudden headache, meningismus, visual disturbances or altered vision, even blindness, and occasionally, decrease in the level of consciousness.

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- Your doctor should be aware if you suffer from a bleeding disorder, thrombocytopenia or if you are on treatment with anticoagulants. Your liver function may need to be monitored as changes to the liver and jaundice (yellow eyes and skin) have been reported with leuporelin treatment.
 - A fractured spine, paralysis, low blood pressure and high blood pressure have been reported with leuporelin treatment.
 - There have been reports of depression in patients taking **Leuporelin 3-month Depot** which may be severe. If you are taking **Leuporelin 3-month Depot** and develop depressed mood, inform your doctor.
 - A decreased bone density (brittleness or thinning of the bones) has been reported with leuporeline. Your doctor may consider adding an antiandrogen to the treatment with **Leuporelin 3-month Depot**. Your doctor will be on the alert for inflamed veins (thrombophlebitis) and other signs of clotting disorders and oedema (swelling of hands, feet or ankles). There is an increased risk of these occurring in the case that an antiandrogen treatment is added to **Leuporelin 3-month Depot**.
 - Tell your doctor, if you feel pressure on the spinal cord and/or experience urinary disorders and/or haematuria (blood in the urine). In this case your doctor will take, if necessary, additional precautions to avoid neurological complications (e.g. tingling in hands and feet, paralysis) or obstruction of the urethra (the tube that connects the bladder to the outside of the body). You will be closely supervised during the first weeks of treatment.
 - Patients may experience metabolic changes (e.g. glucose intolerance or worsening of existing diabetes), weight changes and cardiovascular disorders.
 - Patients with metabolic or cardiovascular disease and especially patients with history of congestive heart failure (condition in which the heart can no longer pump enough blood to the rest of the body) should be monitored during treatment with leuporelin.
 - You will need some blood tests during treatment, to check that **Leuporelin 3-month Depot** is being efficacious.
 - You may experience a loss of interest in sexual intercourse, hot flushes and occasionally there may be a reduction in size and function of the testes.
 - You may become fertile again when **Leuporelin 3-month Depot** treatment is stopped.
 - **Leuporelin 3-month Depot** may interfere with certain laboratory tests so make sure your doctor knows you are using **Leuporelin 3-month Depot**
 - Convulsions can occur in predisposed patients (those with a history of seizures, epilepsy, cerebrovascular disorders, anomalies or central nervous system tumors), in patients



receiving drugs that can cause seizures and, to a lesser extent, in other patients who do not have these characteristics.

- Please tell your doctor if you have any of the following: Any heart or blood vessel conditions, including heart rhythm problems (arrhythmia), or are being treated with medicines for these conditions. The risk of heart rhythm problems may be increased when using **Leuprorelin 3-month Depot**.

Other medicines and **Leuprorelin 3-month Depot**

Tell your doctor or pharmacist if you are taking, have recently taken, or might take any other medicines. It may still be all right for you to be given **Leuprorelin 3-month Depot** and your doctor will be able to decide what is suitable for you.

Leuprorelin 3-month Depot might interfere with some medicines used to treat heart rhythm problems (e.g. quinidine, procainamide, amiodarone and sotalol) or might increase the risk of heart rhythm problems when used with some other drugs (e.g. methadone (used for pain relief and part of drug addiction detoxification), moxifloxacin (an antibiotic), antipsychotics used for serious mental illnesses).

Pregnancy and breast-feeding

Leuprorelin 3-month Depot is not indicated for use in women.

This medicine is contraindicated during pregnancy. Spontaneous abortions may occur if this medicine is administered during pregnancy.

Driving and using machines

No specific studies on the effects of **Leuprorelin 3-month Depot** on the ability to drive and use machines have been performed.

Disturbance of vision and dizziness can occur during treatment. If affected you should not drive or operate machinery.

Leuprorelin 3-month Depot contains less than 1 mmol sodium (23 mg) per dose, i.e. essentially 'sodium-free'.

3. How to use **Leuprorelin 3-month Depot**

Dose

Leuprorelin 3-month Depot must be given under the supervision of a doctor or a qualified health practitioner.

Adults including the elderly:

The recommended dose of **Leuprorelin 3-month Depot** is an injection once every three months. The powder is made up into a suspension and given as a single injection intramuscularly (into a muscle) once every three months

The injection site should be varied at regular intervals.

Leuprorelin 3-month Depot must be administered via the intramuscular route only. Do not administer by another route.

The strength of your treatment is decided by your doctor.

Use in children: **Leuprorelin 3-month Depot** is not indicated for use in children.

If you use more **Leuprorelin 3-month Depot than you should**

This is unlikely as your doctor or nurse will know the correct dosage. However, if you suspect you have received more than you should, let your doctor know about it immediately so appropriate measures can be taken.

If you forget a dose of **Leuprorelin 3-month Depot**

It is important not to miss a dose of **Leuprorelin 3-month Depot**. As soon as you realise you have missed an injection contact your doctor who will be able to give you your next injection.

If you stop using **Leuprorelin 3-month Depot**

Since the medical treatment involves administration of **Leuprorelin 3-month Depot** for a long period, when the treatment is interrupted you may experience a worsening of the symptoms related to the disease. Therefore you must not interrupt the treatment prematurely without your doctor's permission.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your doctor straight away if you get any sudden wheeziness, difficulty in breathing, swelling of the eyelids, face or lips, rash or itching (especially affecting your whole body).

The following side effects have been reported:

Very common (These may affect more than 1 in 10 people):

Hot flushes and injection site reactions.

Common (These may affect up to 1 in 10 people):

Cold sweats, hyperhidrosis (increased sweating), pruritus (itching), fatigue, insomnia (not sleeping), decreased sex drive, spinning sensation (dizziness), flushing, feeling sick (nausea), diarrhoea, , decreased appetite, erectile dysfunction, asthenia (lack or loss of strength), bone pain, pain in the joints and injection site reactions such as pain, induration, erythema (redness of the skin). Urinary tract pain, urine flow decreased, frequent need to urinate, mood changes and depression in long term use of leuporelin, changes in liver enzymes and, blood triglyceride increased (high levels of blood lipids), blood sugar increased.

Uncommon (These may affect up to 1 in 100 people):

High cholesterol, sleep disorders, feeling jittery, taste disturbance, formication (alteration in the skin sensation), headache, lethargy (sleepiness), vision blurred, pleurisy, ringing in the ears (tinnitus), tummy pain upper, constipation, papule, rash, pruritus generalised (itching), night sweats, back pain, muscle aching, neck pain, nipple pain, pelvic pain, testicular atrophy, testicular disorder, feeling hot, mood changes depression in short term use of leuporelin. Changes in blood values and changes in ECG (QT prolongation). And injection site reactions such as: urticaria, warmth and hemorrhage.

Not known (frequency cannot be estimated from available data)

Inflammation of lungs, lung disease

Reporting of side effects

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects **not listed in this leaflet**. You can also report side effects directly via **the**

national reporting system. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store **Leuporelin 3-month Depot**

Your doctor or pharmacist will know how to store **Leuporelin 3-month Depot**.

Keep this medicine out of sight and reach of children.

Do not store above 25° C. Do not freeze.

Do not use this medicine after the expiry date which is stated on the box, vial and pre-filled syringe after "EXP". The syringe has the same expiry date to that of the vial. The expiry date refers to the last day of that month.

Do not throw away any medicines via wastewater. Ask your pharmacist how to throw away medicines you no longer use. These measures will help to protect the environment.

6. Contents of the pack and other information

What **Leuporelin 3-month Depot** contains

The active substance is leuporelin acetate. Each vial contains 22.5 mg of leuporelin acetate.

The concentration of the reconstituted product is 11.25 mg/ml.

The other ingredients are: Polysorbate 80, Mannitol (E-421), Carmellose sodium (E-466), Triethyl citrate and Poly(lactic acid) (PLA).

The solvent contains (pre-filled syringe): mannitol, water for injection, sodium hydroxide (for pH adjustment) and hydrochloric acid (for pH adjustment).

What **Leuporelin 3-month Depot** looks like and contents of the pack

Each pack contains a vial with 22.5 mg of leuporelin acetate, one prefilled syringe with 2 ml of solvent, one adaptor system and one sterile 20 gauge needle.

Marketing Authorisation Holder

GP-PHARM, S.A.
Pol ind Els Vinyets –els Fogars. Sector 2
Carretera comarcal 244, km22
08777 Sant Quintí de Mediona.
Spain

Manufacturer

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Pol ind Els Vinyets –els Fogars. Sector 2
Carretera comarcal 244, km22
08777 Sant Quintí de Mediona.
Spain

This medicinal product is authorised in the Member States of the EEA under the following names:

Spain: Lutrate Depot Trimestral 22.5 mg polvo y disolvente para suspensión de liberación prolongada inyectable
Germany: Lutrate Depot 22.5 mg pulver und lösungsmittel zur Herstellung einer Depot-Injektionssuspension
Portugal: Lutrate Depot 22.5 mg / 2 ml pó e veículo para suspensão injectável de libertação prolongada
Greece: Lutrate Depot 22.5 mg Κόνις και διαλύτης για παρασκευή ενεσίμου εναιωρήματος παρατεταμένης αποδέσμευσης
Italy: Polirate.
Sweden: Polirate 22.5 mg pulver och vätska till injektionväska, suspension
Hungary: Polirate Depot 22.5 mg
Denmark: Lutrate Depot
Finland: Lutrate 22.5 mg
Ireland: Leuprorelin 3-month Depot 22.5 mg powder and solvent for prolonged-release suspension for injection
United Kingdom: Polirate Depot 22.5 mg powder and solvent for prolonged-release suspension for injection

Belgium: Lutrate Depot 22.5 mg poeder en oplosmiddel voor suspensie voor injectie met verlengde afgifte

The Netherlands: Leuproreline Lutrate Depot 22,5 mg poeder en oplosmiddel voor suspensie voor injectie met verlengde afgifte

Norway: Lutrate Depot

Austria: Lutrate Depot 22.5 mg pulver und lösungsmittel zur herstellung einer Depot-injektionssuspension

Estonia: Lutrate Depot 22.5 mg

Lithuania: Lutrate Depot 22.5 mg milteliai ir tirpiklis pailginto atpalaidavimo injekcinei

Latvia: Lutrate Depot 22.5 mg pulveris un šķīdinātājs ilgstošas darbības injekciju suspensijas pagatavošanai

Czech Republic: Lutrate Depot 22.5 mg

Poland: Lutrate Depot

Slovak Republic: Lutrate Depot 22.5 mg

Romania: Lutrate Depot 22.5 mg pulbere și solvent pentru suspensie injectabilă cu eliberare prelungită

Bulgaria: Лутрат Депо 22,5 mg прах и разтворител за инжекционна суспензия с удължено освобождаване

This leaflet was last revised in 08/2018

The following information is intended for healthcare professionals only:

How to prepare the injection?

Follow these instructions carefully.

An aseptic technique should be observed during the reconstitution procedure.

Important:

Once mixed, the product must be administered immediately.

This product is for single use only.

Verify the contents of the kit and make sure it includes everything that's mentioned in the leaflet.

The pack contains:

- 1 (one) vial of **Leuprorelin 3-month Depot** 22.5 mg (leuprorelin acetate) powder for suspension for injection
- 1 (one) pre-filled syringe containing the suspension solvent (mannitol 0.8% solution for injection);
- 1 (one) device for reconstitution containing 1 (one) single-use sterile needle.

1



Remove cap from the vial

2



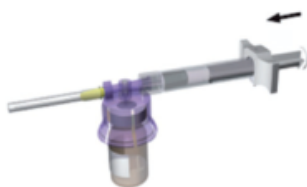
Attach the adaptor system (in purple) to vial until a 'clicking' sound is heard

3



Affix the white finger-grip to the diluents-containing syringe. Remove the rubber cap from the syringe and attach it to the adaptor system

4



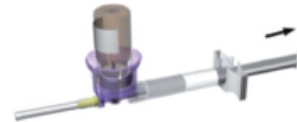
While keeping the syringe and vial securely coupled in an upright position, slowly push the plunger in order to transfer all the diluent into the vial

5



With the syringe still coupled to the vial, shake the vial gently for approximately one minute until a uniform milky-white suspension is obtained

6



Turn the system upside down, and carefully pull out the plunger to draw-up the resuspended drug from the vial into the syringe

7



Detach the syringe and needle from the adaptor system by twisting the upper piece of the adaptor counter-clockwise. The drug is ready to be used.

8



Clean the injection area with an alcohol swab and let the skin dry. Inject the suspension intramuscularly into the upper outer quadrant of the gluteus



Some product may cake or clump at the vial wall. This is considered normal. During the manufacture of the product the vial is filled with excess product in order to make sure that a final dose of 22.5 mg of leuprorelin acetate is administered.