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

The medicine is dispensed with a doctor's prescription only

SUPREFACT DEPOT 3 MONTHS

Implant for subcutaneous injection

SANOFI

Active ingredient

Each syringe, which contains three implant strips, includes:

Buserelin acetate 9.9 mg (equivalent to 9.45 mg buserelin)

Inactive ingredients: see section 6.

Read this leaflet carefully in its entirety before using the medicine.

Keep this leaflet; you may need to read it again.

This leaflet contains concise information about the medicine.

If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

This medicine is intended for men only.

1. WHAT IS THE MEDICINE INTENDED FOR?

To treat prostate cancer.

The medicine acts by lowering testosterone hormone levels.

Therapeutic group: GnRH – Gonadotropin releasing hormone analog.

2. BEFORE USING THE MEDICINE

☒ Do not use the medicine:

- If you are sensitive to buserelin, to other GnRH analogs, to LHRH analogs or to any of the other ingredients of the medicine (see section 6). Signs of an allergic reaction include: rash, swallowing or breathing problems, swelling of the lips, face, throat or tongue.
- If the tumor is resistant to hormonal treatment.
- After surgical removal of the testicles.
- This medicine is intended for men only. Use in women is prohibited.

Special warnings regarding use of the medicine

! Before treatment with the medicine, tell the doctor if:

- you are suffering, or have suffered in the past, from: depression, hypertension, diabetes (see Tests and follow-up section).
- you are sensitive to any food or medicine.
- you are suffering from problems in the nervous system.
- you have difficulties passing urine.
- you have a drop in red blood cell counts (anemia) or are suffering from increased fatigue.

There are reports of depression that may be severe in patients treated with this therapeutic group (GnRH analogs).

If you are being treated with the medicine and develop a depressed mood, refer to a doctor.

Use of preparations in this therapeutic group (GnRH analogs) may cause reduced bone density, osteoporosis, and increased risk of bone fractures. The risk of fractures increases with increased duration of treatment with the preparation.

Tell the doctor if you are suffering from a metabolic bone disease or if you have additional risk factors for osteoporosis, such as chronic alcohol consumption, smoking, familial history of osteoporosis or if you are being treated for a long time with anticonvulsants or corticosteroids.

Use of preparations from this therapeutic group (GnRH analogs) may increase the risk of cardiovascular diseases (such as myocardial infarction, sudden death and stroke, prolongation of the QT interval that is detected in an E.C.G. test), diabetes or anemia (decreased red blood cell count, that causes fatigue).

Use of the preparation can cause positive doping test results; in addition, use of the preparation as a doping agent can put your health at risk.

These risks should be evaluated before starting treatment and you should be under medical surveillance during the course of treatment.

! Other medicines and Suprefact Depot 3 Months

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

In particular, inform the doctor or pharmacist if you are taking:

- Medicines to treat diabetes. Suprefact Depot 3 Months may affect the activity of these medicines, which can lead to worsening of diabetes.
- Medicines that affect the heart rhythm, such as medicines that lead to prolongation of the QT interval in E.C.G or antiarrhythmics (such as quinidine, disopyramide, amiodarone, sotalol, procainamide, dofetilide, ibutilide) or methadone, moxifloxacin and antipsychotics.

! Driving and operating machinery

Use of this medicine may impair alertness and therefore requires that caution be exercised when driving a car, operating dangerous machinery and when engaging in any activity that requires alertness.

3. HOW SHOULD YOU USE THE MEDICINE?

Dosage is according to the doctor's instructions only.

The preparation is intended for long-term treatment. The duration of treatment will be determined by the doctor.

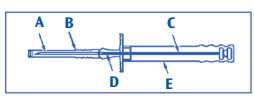
The doctor or nurse will inject the entire content under the skin every 3 months.

The 3-month interval may be extended by up to 3 weeks.

The doctor may decide to start antiandrogen treatment approximately 5 days before starting treatment with Suprefact Depot 3 Months and to continue it in parallel to treatment with Suprefact Depot 3 Months for a period of 3-4 weeks (see section 4. Side Effects), especially in patients with metastases.

Instructions for use

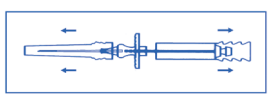
Attention: To prevent the implant strips from falling out of the syringe needle (A), hold the syringe vertically, with the needle pointing upward, until just before the injection.



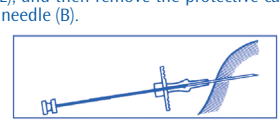
A. Needle
B. Protective cap of needle
C. Plunger
D. Implant
E. Protective cap of plunger

1. After opening the pack and removing the syringe from the wrapping, check that the implants are located in the window of the handle (D). If necessary, gently tap the protective cap on the needle (B) with the finger to position the implants in the window.

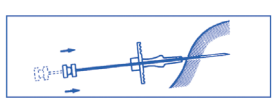
The syringe should be used immediately after removing it from the wrapper.



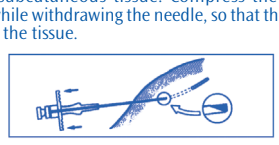
2. Disinfect the injection site in the area of the lateral side wall of the abdomen. Remove the protective cap from the plunger (E), and then remove the protective cap from the injection needle (B).



3. Lift a skinfold, and insert the needle approximately 3 cm into the subcutaneous tissue, holding the syringe in a horizontal position or with the tip of the needle pointed slightly upwards immediately prior to injection. Pull the syringe back about 1-2 cm prior to injection of the implants.



4.Fully depress the plunger (C) in order to inject the implants into the subcutaneous tissue. Compress the puncture channel while withdrawing the needle, so that the implants remain in the tissue.



5. To ensure that all three implants have been injected, check the tip of the plunger and see if the implants are visible at the tip of the needle.

Tests and follow-up

- During the course of treatment, blood tests should be performed regularly to check if the medicine is working.
- Use of Suprefact Depot 3 Months may affect blood test results. The change can be especially manifested by increased liver enzyme and lipid levels in the blood. If you are due to undergo blood tests, inform your doctor.
- Patients with metastases in the spinal cord, patients with nervous system complications or patients with an obstruction in the urinary system should be under tight medical surveillance during the first few weeks of treatment if they are not receiving antiandrogenic treatment.
- If you are being concomitantly treated with medicines that can affect the heart rhythm (see section 2), E.C.G. monitoring should be performed.
- If you are suffering, or have suffered in the past, from depression – your mental state should be monitored and you should receive appropriate treatment, if necessary.
- Patients with hypertension – blood pressure tests should be performed regularly during the course of treatment with this medicine.
- Patients with diabetes – blood sugar tests should be performed regularly.
- It is recommended to periodically perform BMD bone density tests and to receive appropriate treatment, if necessary.
- Use of the preparation may cause positive doping test results.

If more Suprefact Depot than necessary was injected:

Such a situation in unlikely. Overdose may cause weakness, nervousness, dizziness, nausea, headache, flushing, abdominal pain, swelling of the ankles and lower part of the legs, chest pain or injection site reactions.

If an overdose has been injected, or if a child has accidentally swallowed 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 forgot to inject Suprefact Depot, consult the doctor.

Adhere to the treatment regimen recommended by the doctor.

Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor.

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

4. SIDE EFFECTS

As with any medicine, use of Suprefact Depot may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them.

Discontinue use and refer to a doctor immediately if:

- you experience a severe allergic reaction. Signs of an allergic reaction include: rash, swallowing or breathing problems, swelling of the lips, face, throat or tongue. There may be a need to remove the implant.
- you are suffering from pains in the legs, breathing problems or shortness or breath and chest pain. This may occur due to formation of blood clots.

At the beginning of the treatment, there is an increase in the levels of sex hormones that your body produces, which can cause temporary worsening of the symptoms, for example:

Occurrence or exacerbation of bone pains in patients suffering from metastases, in rare cases, a mild and temporary increase in pain in the tumor area, muscle weakness in the legs, disturbances in passing of urine, fluid retention, dilation of the renal pelves or lymphatic disturbance, excessive blood clotting and pulmonary embolism.

Most of these effects can be avoided by starting antiandrogen treatment approximately 5 days before starting treatment with Suprefact Depot. The concomitant treatment can be continued for 3-4 weeks. After this time, the testosterone levels usually decline back to the desired range.

Additional side effects:

Refer to a doctor if any of the following effects worsen or continue for more than a few days:

Common side effects (occur in at least 1-10 in 100 users):

- loss of sexual drive
- difficulty sustaining an erection
- headache
- hot flushes
- shrinking of the testicles
- pain or other injection site reactions (redness or swelling)
- mood changes, depression (with prolonged treatment)

Uncommon side effects (occur in at least 1-10 in 1,000 users):

- hypersensitivity reactions, such as skin rash, that may be reddish and itchy (including urticaria)
- drowsiness or fatigue
- dizziness
- constipation
- breast enlargement
- edema in the ankles and lower parts of the legs
- increased liver enzymes levels (shown in blood tests)
- change in body weight
- mood changes, depression (with short-term treatment)

Rare side effects (occur in at least 1-10 in 10,000 users):

- severe hypersensitivity reactions, such as shortness of breath. In cases of an anaphylactic/anaphylactoid reaction, the implant may have to be surgically removed
- nervousness, stress and mood changes, sleep disturbances and memory or concentration problems
- irregular or fast heartbeats, rise in blood pressure in patients who already have high blood pressure
- nausea, vomiting or diarrhea
- increase or decrease in the amount of hair on the head and body
- changes in blood lipid levels and increased serum bilirubin levels, shown in blood tests

Very rare side effects (occur in less than one in 10,000 users):

- discomfort and even pains in the muscles and bones. Prolonged use of the preparation may increase the risk of development of osteoporosis, a condition associated with increased risk of bone fractures
- severe hypersensitivity reactions, such as shock
- increased thirst, changes in appetite, reduced glucose tolerance (that in diabetic patients can lead to loss of control of blood sugar levels)
- ringing in the ears, changes in hearing
- eyesight disturbances (blurred vision) and feeling of pressure behind the eyes
- discomfort or pain in the muscles or musculoskeletal system
- deterioration of general well-being
- lowering of platelet count (thrombopenia), that can lead to abnormal blood test results and/or bruising
- lowering of white blood cell counts (leucopenia)
- enlargement of benign tumors in the pituitary gland or temporary increase in cancer-associated pain.

Side effects that occurred at an unknown frequency: prolongation of the QT interval that is shown in E.C.G tests (heart rhythm problem).

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

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine and any other medicine should be kept in a safe place out of the reach of children and/or infants in order to avoid poisoning. Do not induce vomiting without explicit instruction from the doctor.

If you took an overdose or if a child has accidentally swallowed the medicine, immediately proceed to a hospital emergency room and bring the package of the medicine with you.

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 above 30°C.

6. FURTHER INFORMATION

In addition to the active ingredient, Suprefact Depot 3 Months also contains Poly-(D,L-Lactide-co-glycolide) 75:25

What the medicine looks like and the contents of the package

The package contains a sealed sachet, which contains a sterile syringe with 3 implant strips.

This leaflet does not contain all the information about your medicine. If you have any questions or are not sure about anything, please ask your doctor.

License holder and address: sanofi-aventis Israel ltd., 10 Beni Gaon Street, Netanya 4250499

Manufacturer's name and address: Sanofi-Aventis, Frankfurt, Germany

This leaflet was checked and approved by the Ministry of Health in August 2015.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 1161829721