This package insert is continually updated: please read carefully before using a new pack!

profact® Depot

Active ingredient: Buserelin acetate

Composition

Each applicator with two identical rods contains, as active ingredient, 6.6 mg buserelin acetate, equivalent to 6.3 mg buserelin.

Excipient: poly-(D,L-lactide-co-glycolide) 75:25.

Properties

Buserelin acetate, the active ingredient of profact Depot, is an analogue of the natural gonadotrophin-releasing hormone (GnRH). In continuous administration, profact Depot results in inhibition of secretion of gonadotrophins and gonadal steroids, leading to a fall in serum testosterone to a level within the castrate range. This level remains stable for two months after each injection. Because of this effect, profact Depot is well-suited for the long-term treatment of prostatic carcinoma.

profact Depot is well tolerated. During the two-month dose interval, the rods undergo slow biodegradation; thereafter, biodegradation accelerates. The resulting monomers, lactic acid and glycolic acid, are naturally-occurring compounds.

Indication

Treatment of advanced hormone-dependent prostatic carcinoma.

Contraindications

Hypersensitivity to buserelin.

After surgical removal of the testes, no further reduction of testosterone levels by profact Depot can be expected.

Special warnings and precautions

It is strongly recommended that administration of an antiandrogen be started as adjunctive therapy about 5 days before starting treatment. This therapy must be continued concomitantly with buserelin therapy for 3 to 4 weeks (see under "Dosage and administration"). After this time, testosterone levels have usually fallen to within the desired range. In patients with known metastases (e.g. of the spinal column), this adjunctive therapy is indispensable to prevent initial complications up to and including, for example, spinal compression and paralysis, arising from a transient activation of the tumour and its metastases (see also under "Adverse effects").

In hypertensive patients, blood pressure must be monitored regularly (risk of increase in blood pressure).

In diabetic patients, blood sugar levels must be checked regularly (risk of deterioration of metabolic control).

Patients with a history of depression must be monitored carefully and, if necessary, treated (risk of recurrence or worsening of depression).

Certain adverse effects (e.g. dizziness) may impair the ability to concentrate and react, and, therefore, constitute a risk in situations where these abilities are of particular importance (e.g. operating a vehicle or machinery).

Adverse effects

At the start of treatment, a transient rise in the serum testosterone levels usually develops and may lead to a temporary activation of the tumour with secondary reactions such as

- occurrence or worsening of bone pain in patients with bone metastases.
- signs of neurologic deficit due to tumour compression with e.g. muscle weakness in the legs.
- impaired micturition, hydronephrosis or lymphostasis.
- thrombosis with pulmonary embolism.

Such reactions can be largely avoided when an antiandrogen is given concomitantly in the initial phase of buserelin treatment (see also under "Special warnings and precautions"). Even then, however, a mild but transient increase in tumour pain as well as a deterioration in general well-being may develop in some patients.

Additionally, as a result of hormone deprivation, hot flushes and loss of potency or libido occur in most patients.

Mild oedemas of the ankles and lower leg may occur as may, occasionally, usually painless gynaecomastia.

Long-term treatment with LHRH agonists may, in isolated cases, lead to development of pituitary adenomas; however, this has not yet been observed in patients treated with buserelin.

Buserelin treatment may lead to

- increase or decrease in scalp or body hair.
- increase in blood pressure in hypertensive patients.
- hypersensitivity reactions. These may become manifest as, e.g. reddening of the skin, itching, skin rashes (including urticaria) and allergic asthma with dyspnoea but may also, in isolated cases, lead to anaphylactic/anaphylactoid shock. If anaphylactic/anaphylactoid reactions occur it may become necessary to remove the implant surgically (as is usual with implants).

- reduction in glucose tolerance (possible deterioration of metabolic control in diabetic patients).
- changes in blood lipids; increase in serum levels of liver enzymes (e.g. transaminases) or in bilirubin; thrombopenia and leucopenia.
- headache, palpitations, nervousness, sleep disturbances, tiredness, drowsiness, disturbances of memory and concentration, emotional instability, feelings of anxiety. In rare cases, depression may develop or existing depression may worsen.
- dizziness, tinnitus, hearing disorders, impaired vision (e.g. blurred vision), feeling of pressure behind the eyes.
- nausea, vomiting, increased thirst, diarrhoea, constipation, changes in appetite, weight changes (increase or decrease).
- back pain and pains in the limbs, joint discomfort.
- local irritation and pain at the site of injection (in about 3% of patients).

Please consult a physician if you notice any of the adverse effects listed in this package insert or any other undesired effects or unexpected changes.
Since some adverse effects (for example, allergic asthma with dyspnoea, anaphylactic/anaphylactoid shock, thrombosis with pulmonary embolism) may under certain circumstances become life-threatening, it is essential that, if sudden or severe reactions do occur, you inform a physician at once.

Interactions
During treatment with buserelin, the effect of antidiabetic agents may be attenuated (see also under "Adverse effects").

Dosage and administration
The contents of the applicator (equivalent to 6.3 mg buserelin) are injected subcutaneously into the abdominal wall every 2 months. The 2-month interval between injections may, however, be shortened or extended by a few days. A local anaesthetic may be used before injection at the discretion of the patient or physician.

Adjunctive therapy: About five days before the first injection of profact Depot, an antiandrogen (e.g. cyproterone acetate, flutamide or nilutamide) should be administered at the manufacturer's recommended dosage, and administration then continued concomitantly over three to four weeks (see under "Special warnings and precautions" and "Adverse effects").
The response to treatment may be monitored by measuring levels of testosterone, acid phosphatase and prostate-specific antigen (PSA) in serum. Testosterone concentration increases at the start of treatment and then decreases over a period of 2 weeks, reaching the castrate range after two to four weeks and remaining there for the duration of treatment.

profact Depot is intended for long-term treatment. The duration of treatment is determined by the physician.

Storage
Store at room temperature (below + 30 °C).

Expiry date
Do not use later than the date of expiry.

Keep medicines out of the reach of children.

Presentation
Sterile disposable applicator containing one implant consisting of two identical rods.

Instructions for Using the Applicator

Please note: To prevent the implant rods from falling out of the injection needle, hold the applicator in a vertical position until immediately prior to puncture, with the needle pointing upwards.

1. After opening the pack and removing the applicator from the wrapping, check that both implants are located in the window of the handle. If necessary, tap the protective cap on the needle lightly with the finger to reposition them in the window.
2. Disinfect the injection site in the area of the lateral abdominal wall. Then, after removing the protective case from the plunger (E), remove the cap from the injection needle (B).
3. Lift a fold of skin, and insert the needle approx. 3 cm (somewhat more than 1 inch) into the subcutaneous tissue, holding the applicator immediately prior to puncture in a horizontal position or with the tip of the needle pointed slightly upwards. Withdraw the applicator about 1 to 2 cm prior to injection of the implants.
4. Fully depressing the plunger, inject the implants into the subcutaneous tissue. Compress the puncture channel while withdrawing the needle, so that the implants are retained in the tissue.
5. To make certain that both implants have been injected check the tip of the plunger to see if it is visible at the tip of the needle.

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