DECAPEPTYL® 0.1 mg/ 1ml solution for injection

2009053849

FERRING PHARMACEUTICALS

QUALITATIVE AND QUANTITATIVE COMPOSITION
Each pre-filled syringe of 1 ml solution for injection contains 100 micrograms triptorelin acetate (1:1) equivalent to 95.6 micrograms triptorelin free base.

PHARMACEUTICAL FORM
Solution for injection
Clear colourless solution

CLINICAL PARTICULARS
Therapeutic indications
IVF:
DECAPEPTYL® is indicated for downregulation and prevention of premature LH (LH = luteinizing hormone) surges in women undergoing controlled ovarian hyperstimulation for assisted reproductive technologies (ART). In clinical trials DECAPEPTYL® has been used in cycles where urinary and recombinant human follicle stimulating hormone (FSH) as well as human menopausal gonadotrophin (HMG) were used for stimulation.
Prostate Cancer:
Therapy: Symptomatic treatment of the advanced hormone-dependent prostate carcinoma.
Diagnosis:Diagnosis of hormone sensibility of a prostate carcinoma within a probatory therapy.

Posology and method of administration
IVF:
Treatment with DECAPEPTYL® should be initiated only under the supervision of a physician experienced in the treatment of infertility. DECAPEPTYL® is intended for subcutaneous injection once daily into the lower abdominal wall. Following the first administration, it is advised that the patient be kept under medical supervision for 30 minutes to ensure there is no allergic/pseudo-allergic reaction to the injection. Facilities for the treatment for such reactions should be immediately available. The following injections may be self-administered as long as the patient is made aware of the signs and symptoms that may indicate hypersensitivity, the consequences of such a reaction and the need for immediate medical intervention.The injection site should be varied to prevent lipoatrophy. Treatment can be started in the early follicular phase (day 2 or 3 of the menstrual cycle) or in the mid-luteal phase (day 21-23 of the menstrual cycle or 5-7 days before expected start of menses). Controlled ovarian hyperstimulation with gonadotrophins should be started after approximately 2-4 weeks of DECAPEPTYL® treatment. Ovarian response should be monitored clinically (including ovarian ultrasound alone or preferably in combination with measurement of oestradiol levels) and the dose of gonadotrophins adjusted accordingly. When a suitable number of follicles have reached an appropriate size, treatment with DECAPEPTYL® and gonadotrophin is stopped and a single injection of hCG is administered to induce the final follicular maturation. If downregulation is not confirmed after 4 weeks (determined by ultrasound documentation of a shedded endometrium alone or preferably in combination with measurement of oestradiol levels), discontinuation of DECAPEPTYL® should be considered. The total duration of treatment is usually 4-7 weeks. When using DECAPEPTYL®, luteal phase support should be provided according to the reproductive medical centre's practice. No specific dose recommendations are given for subjects with renal or hepatic impairment. A clinical study indicated that the risk of accumulation of triptorelin in patients with severe liver and renal impairment is small.
Prostate Cancer:
Dosage: Initially, triptorelin 0.5 mg is administered once a day for 7 days. From the 8th day on, DECAPEPTYL 0.1 mg is administered once a day.

Method and duration of administration
DECAPEPTYL 0.1 mg is injected subcutaneously. DECAPEPTYL is foreseen for long-term treatment. The duration of therapy is fixed by the physician in charge.

Contraindications
DECAPEPTYL® is contraindicated in cases of:
- Hypersensitivity to the active substance or to any of the excipients
- Hypersensitivity to gonadotrophin-releasing hormone (GnRH) or any other GnRH analogue
- Pregnancy and Lactation period

- In case the carcinoma is hormone-independent, treatment with DECAPEPTYL is not indicated. Following surgical castration, DECAPEPTYL induces no further decrease in the testosterone level.
- Known hypersensitivity against triptorelin or another ingredient of the drug

Special warnings and precautions for use
The use of GnRH agonists may cause reduction in bone mineral density. In men, preliminary data suggest that the use of a bisphosphonate in combination with an GnRH agonist may reduce bone mineral loss. Particular caution is necessary in patients with additional risk factors for osteoporosis (e.g. chronic alcohol abuse, smokers, long-term therapy with drugs that reduce bone mineral density, e.g. anticonvulsants or corticoids, family history of osteoporosis, malnutrition).

Loss of bone mineral density
The use of GnRH agonists is likely to cause reduction in bone mineral density averaging 1% per month during a six month treatment period. Every 10% reduction in bone mineral density is linked with about a two to three times increased fracture risk. In the majority of women, currently available data suggest that recovery of bone loss occurs after cessation of therapy. No specific data is available for patients with established osteoporosis or with risk factors for osteoporosis (e.g. chronic alcohol abuse, smokers, long-term therapy with drugs that reduce bone mineral density, e.g. anticonvulsants or corticoids, family history of osteoporosis, malnutrition, e.g. anorexia nervosa). Since reduction in bone mineral density is likely to be more detrimental in these patients, treatment with triptorelin should be considered on an individual basis and only be initiated if the benefits of treatment outweigh the risk following a very careful appraisal. Consideration should be given to additional measures in order to counteract loss of bone mineral density. After withdrawal of treatment, the bone loss is generally reversible within 6 - 9 months. It should be confirmed that the patient is not pregnant before prescription of triptorelin. Rarely, treatment with GnRH agonists may reveal the presence of a previously unknown gonadotroph cell pituitary adenoma. These patients may present with a pituitary apoplexy characterised by sudden headache, vomiting, visual impairment and ophthalmoplegia. There is an increased risk of incident depression (which may be severe) in patients undergoing treatment with GnRH agonists, such as triptorelin. Patients should be informed accordingly and treated as appropriate if symptoms occur. Mood changes, including depression have been reported. Patients with known depression should be monitored closely during therapy. Ovarian stimulation should be done under strict medical supervision. In patients with renal or hepatic impairment, triptorelin has a mean terminal half life of 7-8 hours compared to 3-5 hours in healthy subjects. Despite this prolonged exposure, triptorelin is not expected to be present in circulation at the time of embryo transfer. Special care should be taken in women with signs and symptoms of active allergic conditions or known history of allergic predisposition. Treatment with DECAPEPTYL® is not advised in women with severe allergic conditions. Women of childbearing potential should be examined carefully before treatment to exclude pregnancy. ART is associated with an increased risk of multiple pregnancies, pregnancy wastage, ectopic pregnancies and congenital malformations. These risks are also valid with usage of DECAPEPTYL® as adjunct therapy in controlled ovarian hyperstimulation. The use of DECAPEPTYL® in controlled ovarian hyperstimulation may increase the risk of ovarian hyperstimulation syndrome (OHSS) and ovarian cysts. Follicular recruitment, induced by the use of GnRH analogues and gonadotrophins, may be markedly increased in a minority of predisposed patients, particularly in case of Polycystic Ovarian Syndrome. As with other GnRH analogues there have been reports of ovarian hyperstimulation syndrome (OHSS) associated with the use of triptorelin in combination with gonadotrophins.

Ovarian Hyperstimulation Syndrome (OHSS):
OHSS is a medical event distinct from uncomplicated ovarian enlargement. OHSS is a syndrome that can manifest itself with increasing degrees of severity. It comprises marked ovarian enlargement, high serum sex steroids, and an increase in vascular permeability which can result in an accumulation of fluid in the peritoneal, pleural and, rarely, in the pericardial cavities.The following symptoms may be observed in severe cases of OHSS: abdominal pain, abdominal distension, severe ovarian enlargement, weight gain, dyspnoea, oliguria and gastrointestinal symptoms including nausea, vomiting and diarrhoea. Clinical evaluation may reveal hypovolaemia, haemoconcentration, electrolyte imbalances, ascites, haemoperitoneum, pleural effusions, hydrothorax, acute pulmonary distress, and thromboembolic events. Excessive ovarian response to gonadotrophin treatment seldom gives rise to OHSS unless hCG is administered to trigger ovulation. Therefore in cases of OHSS it is prudent to withhold hCG and advise the patient to refrain from coitus or to use barrier methods for at least 4 days. OHSS may progress rapidly (within 24 hours to several days) to become a serious medical event, therefore patients should be followed for at least two weeks after the hCG administration. OHSS may be more severe and more protracted if pregnancy occurs. Most often, OHSS occurs after hormonal treatment has been discontinued and reaches its maximum severity at about seven to ten days following treatment. Usually, OHSS resolves spontaneously with the onset of menses. If severe OHSS occurs, gonadotrophin treatment should be stopped if still ongoing, the patient hospitalised and specific therapy for OHSS started e.g. with rest, intravenous infusion of electrolyte solutions or colloids and heparin. This syndrome occurs with higher incidence in patients with polycystic ovarian disease. The risk of OHSS might be higher with use of GnRH agonists in combination with gonadotrophins than with use of gonadotrophins alone.

Ovarian cysts:
Ovarian cysts may occur during the initial phase of treatment with GnRH agonist. They are usually asymptomatic and non-functional.
DECAPEPTYL® contains sodium, but less than 1 mmol (23 mg) sodium per maximum dose.

Interaction with other medicinal products and other forms of interaction
Interactions of DECAPEPTYL® with other medicines have not been investigated for this indication. The possibility of interactions with commonly used medicinal products, including histamine liberating products, cannot be excluded. When triptorelin is co-administered with drugs affecting pituitary secretion of gonadotrophins caution should be given and it is recommended that the patient's hormonal status should be supervised. For theoretical consideration, interference of calcium antagonists with the mechanism of action of GnRH and GnRH-analogues may be possible. However, first test results with triptorelin on long-term suppressibility of the serum testosterone with simultaneous therapy with calcium antagonists did not show any indication for such an interaction

Pregnancy and lactation
Pregnancy
DECAPEPTYL® is not indicated during pregnancy. Pregnancy must be excluded before initiation of fertilisation treatment. Non-hormonal methods of contraception should be employed during therapy until menses resume. If a patient becomes pregnant while receiving triptorelin, therapy should be discontinued. When triptorelin is used for fertilisation treatment, there is no clinical evidence to suggest a causal connection between triptorelin and any subsequent abnormalities of oocyte development or pregnancy or outcome. Very limited data on the use of triptorelin during pregnancy do not indicate an increased risk of congenital malformations.
Studies in animals have shown reproductive toxicity.
Based on the pharmacological effects disadvantageous influence on the pregnancy and the offspring cannot be excluded.
Lactation
DECAPEPTYL® is not indicated for use during lactation.

Effects on ability to drive and use machines
No studies on the effects on the ability to drive and use machines have been performed. However, due to its pharmacological profile DECAPEPTYL® is likely to have no or negligible influence on the patient's ability to drive and use machines.

Undesirable effects
At the beginning of treatment with DECAPEPTYL®, the combination with gonadotrophins may result in ovarian hyperstimulation syndrome. Ovarian enlargement, dyspnoea, pelvic and/or abdominal pain may be observed.
Genital haemorrhage including menorrhagia and metrorrhagia may occur at the beginning of treatment with DECAPEPTYL®.
During treatment with triptorelin some adverse reactions showed a general pattern of hypo-oestrogenic events related to pituitary-ovarian blockade such as sleep disorder, headache, mood altered, vulvovaginal dryness, dyspareunia and libido decreased. Breast pain, muscle spasms, arthralgia, weight increased, nausea, abdominal pain, abdominal discomfort, asthenia and episodes of blurred vision and visual disturbances may occur during treatment with DECAPEPTYL®.
Single cases of allergic reactions, localized or generalized, have been reported after injection of DECAPEPTYL®.

IVF:
Very common: Headache, abdominal pain, nausea, vaginal haemorrhage, injection site inflammation.
Common: Upper respiratory tract infection, pharyngitis, dizziness, hot flushes, abdominal distension, vomiting, back pain, abortion, pelvic pain, ovarian hyperstimulation syndrome, dysmenorrhoea, ovarian cyst, injection site pain, injection site reaction, fatigue, influenza like illness.
Uncommon: Mood changes, depression.
Not known: Hypersensitivity, sleep disorder, libido decreased, visual impairment, vision blurred, dyspnoea, abdominal discomfort, hyperhidrosis, pruritus, rash, angioedema, urticaria, muscle spasms, arthralgia,ovarian enlargement, menorrhagia, metrorrhagia, vulvovaginal dryness, dyspareunia, breast pain, asthenia, injection site erythema, weight increased.

Prostate cancer:
Very common: The androgen suppression very often leads to hot flushes with sweating, loss of libido and potency.
Uncommon: Gynaecomastia, testicular atrophy and sleep disturbances.
Very rare: In single cases, headache and thrombophlebitis have been reported. One patient suffered a pulmonary embolism.
As with other peptides, hypersensitivity reactions (e.g. itching, skin rash, fever, anaphylaxis) may occur in individual cases.

Overdose
IVF:
Overdose in humans may result in a prolonged duration of action. In case of overdose, DECAPEPTYL® treatment should be (temporarily) discontinued.
No adverse reaction has been reported as a consequence of overdose.
Prostate Cancer:
Symptoms of intoxication: Due to the broad therapeutic scope of the active ingredient triptorelin, overdosages and intoxications are not to be expected.
Therapy of intoxications: A specific antidote for DECAPEPTYL is not known.

PHARMACEUTICAL PARTICULARS
List of excipients
Sodium chloride
Acetic acid 99% (for pH adjustment)
Water for injections

Incompatibilities: In the absence of incompatibility studies, the medicinal product must not be mixed with other medicinal products.

Shelf life: See outer carton.

Special precautions for storage: Store in a refrigerator (2°C – 8°C). Do not freeze. Store in the original package, to protect from light.

Nature and contents of container:1 ml solution in a pre-filled syringe (glass) with plunger stopper (chlorobutyl rubber), plunger rod (polystyrene), integrated needle and rigid needle shield in pack size of 7.

Special precautions for disposal: Inject the entire contents of a pre-filled disposable syringe subcutaneously. Single-use only. No special requirements for disposal.

MANUFACTURER & MARKETING AUTHORISATION HOLDER
Ferring GmbH
Wittland 11, D-24109
Kiel, Germany.

Prescription/pharmacy status
Prescription only

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October 2013

THIS IS A MEDICINE
- A MEDICINE IS A PRODUCT WHICH AFFECTS YOUR HEALTH, AND ITS CONSUMPTION CONTRARY TO INSTRUCTIONS IS DANGEROUS FOR YOU.
- STRICTLY FOLLOW THE DOCTOR'S PRESCRIPTION, THE METHOD OF USE AND THE INSTRUCTIONS OF THE PHARMACIST WHO SOLD THE MEDICINE.
- THE DOCTOR AND THE PHARMACIST ARE EXPERTS IN MEDICINE, ITS BENEFITS AND RISKS.
- DO NOT BY YOURSELF INTERRUPT THE PERIOD OR TREATMENT PRESCRIBED FOR YOU.
- DO NOT REPEAT THE SAME PRESCRIPTION WITHOUT CONSULTING YOUR DOCTOR.
- KEEP THE MEDICINE OUT OF REACH OF CHILDREN.

Council of Arab Health Ministers
Union of Arab Pharmacists