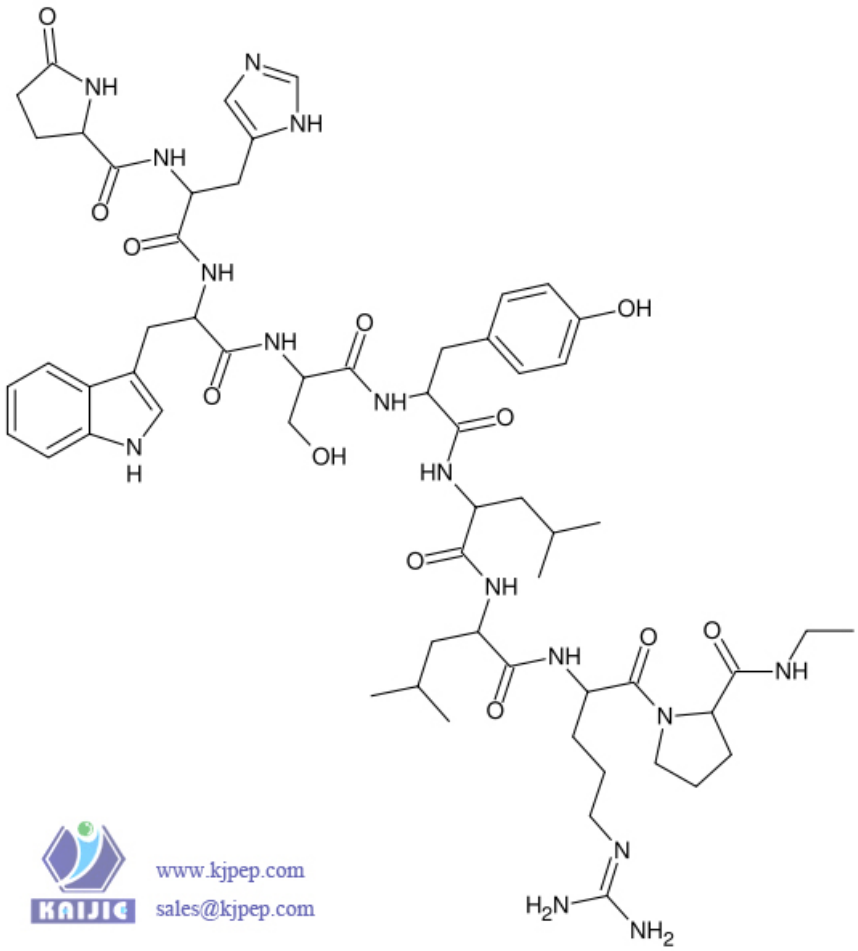
Chengdu KaiJie Biopharm Co., Ltd.

Segment 1, Industrial Road, Dayi county, Chengdu, Sichuan, P. R. China，611330
Tel： 86-28-88203603，Fax： 86-28-88203605 WEB: www.kjpep.com

About Author

Chengdu Kaijie Biopharm Co, Ltd. (KJBP) is one of leading peptide manufacturers in Asia. With its highest capacity of production in China and the outstanding quality of peptide products, Kaijie holds a unique position.

Leuprolide



Leuprorelin

1.1. A.1 Intramuscular route

1.1. A.1.a Anemia - Uterine leiomyoma, Preoperatively, with iron therapy

1) The recommended dose of Lupron Depot(R) for uterine leiomyomata is 3.75 milligrams intramuscularly monthly for a maximum of 3 months. Therapy should be given concomitantly with iron. The clinician may wish to consider a 1-month trial period of iron only. Leuprolide may be added if the response to iron alone is inadequate

2) The recommended dose of Lupron Depot(R)-3 Month for uterine leiomyomata is 11.25 milligrams given as one intramuscular injection. Therapy should be given concomitantly with iron. This dosage form is indicated only for women for whom 3 months of hormonal suppression is deemed necessary.

3) The symptoms of uterine leiomyomata will reoccur following discontinuation of therapy. If additional treatment with leuprolide is contemplated, bone density should be assessed prior to initiation of therapy to ensure that values are within normal limits

1.1. A.1.b Endometriosis

1) The recommended dose of leuprolide (DEPOT FORMULATION) for endometriosis is 3.75 milligrams given by intramuscular injection monthly. The manufacturer recommends limiting treatment to 6 months, and that bone density be determined before attempting retreatment. Safety data for retreatment is not available.

2) The recommended dose of Lupron Depot(R)-3 Month is 11.25 milligrams in one intramuscular injection every 3 months for a maximum recommended duration of 6 months. Retreatment is not recommended by the manufacturer since safety data is lacking. However, if the symptoms of endometriosis reoccur after a course of therapy, and further treatment is necessary, then it is recommended that bone density be assessed before retreatment begins.

1.1. A.1.c Premenstrual syndrome

1) For the symptoms of premenstrual syndrome, a dose of leuprolide 3.75 mg IM depot injection once monthly for 3 months has been used .

1.1. A.1.d Prostate cancer, Advanced (palliative treatment)

1) Lupron Depot 7.5 milligrams(R) should be administered monthly as an intramuscular injection. This may be continued indefinitely if efficacy continues.

2) The recommended dose of Lupron Depot(R)-3 Month is 22.5 milligrams to be administered as one injection every 3 months or 84 days. Of note is that a fractional dose of this 3-month depot formulation is not equivalent to the same dose of the monthly formulation and should not be given as such.

3) The recommended dose of Lupron Depot(R)-4 Month is 30 milligrams to be administered as one injection every 4 months or 16 weeks. Of note is that a fractional dose of this 4-month depot formulation is not equivalent to the same dose of the monthly formulation and should not be given as such

1.1. A.2 Subcutaneous route

1.1. A.2.a Female infertility

1) Leuprolide 1 milligram subcutaneously each day for 4 weeks followed by human menopausal gonadotropins (hMG) (various individualized doses and schedules) has been

reported effective in preventing premature luteinization during hMG induction of ovulation in females with polycystic ovary syndrome

1.1. A.2.b In vitro fertilization

1) Single subcutaneous half-doses of leuprolide depot may be an appropriate alternative to daily subcutaneous doses of short-acting leuprolide for pituitary suppression in ovarian stimulation for in-vitro fertilization. Single doses of leuprolide depot (1.88 milligrams (mg) subcutaneously started on cycle day 21 to 23) produced similar results as short-acting leuprolide (0.5 mg/day started on cycle day 21 to 23) in a RETROSPECTIVE study of 447 patients receiving controlled ovarian hyperstimulation, in-vitro fertilization, and transvaginal embryo transfer. No statistically significant differences in number of oocytes retrieved, number of oocytes fertilized and embryos transferred, and pregnancy rates were reported between the two groups

1.1. A.2.c Prostate cancer, Advanced (palliative treatment)

1) Daily Injection
- **a)** The usual dose of Lupron (R) is 1 milligram subcutaneously daily

2) Monthly Implant
- **a)** The monthly subcutaneous (subQ) formulation (Eligard(R)) is administered as a 7.5 mg subQ depot injection once monthly.

3) Yearly Implant
- **a)** Leuprolide acetate implant (Viadur(R)) should be inserted subcutaneously in the inner area of the upper arm once every 12 months for the palliative treatment of advanced prostate cancer. One leuprolide acetate implant delivers 120 micrograms of leuprolide acetate daily for 12 months

2. Pediatric Dosage

2.1. A.1.a Central precocious puberty

1) The recommended starting dose of leuprolide (depot formulation) for precocious puberty is 0.3 milligrams/kilogram every 4 weeks intramuscularly, with a minimum dose of 7.5 milligrams. The following ranges are recommended: children weighing 25 kg or less, 7.5 mg; children weighing 25 to 37.5 kg, 11.25 mg; children weighing greater than 37.5 kg, 15 mg. If the starting dose of leuprolide does not result in total downregulation, the dose can be titrated upward by 3.75 milligrams every 4 weeks.

2) The first dose found to result in adequate downregulation can probably be maintained for the duration of therapy in most children. However, in a child that has had a significant weight gain, it is recommended that the downregulation be verified. Discontinuation of leuprolide should be considered before age 11 for females and age 12 for males.

2.1.A.2 Subcutaneous route

2.1. A.2.a Central precocious puberty

1) The recommended starting dose of leuprolide for precocious puberty is 50 micrograms/kilogram/day given subcutaneously. If this dose does not result in total downregulation, the dose can be titrated upward by 10 micrograms/kilogram/day.

2) The first dose found to result in adequate downregulation can probably be maintained for the duration of therapy in most children. However, in a child that has had a significant weight gain, it is recommended that the downregulation be verified. Discontinuation of leuprolide should be considered before age 11 for females and age 12 for males

3.0 Pharmacokinetics

3.1 Onset and Duration

A) Onset

1) Initial Response

a) Prostatic carcinoma, subcutaneous injection: 12 weeks (Anon, 1984).

1) TESTOSTERONE SUPPRESSION: Decreases in serum testosterone levels with daily subcutaneous injections of leuprolide appear to be greatest after 2 to 4 weeks of treatment. Decreases in serum testosterone levels are preceded by transient increases, occurring during the first week of treatment; peak increases in plasma testosterone appear to occur at 72 hours with daily subcutaneous injections and may be associated with increases in bone pain and obstructive symptoms secondary to tumor stimulation

2) FSH/LH SUPPRESSION: Decreases in follicle-stimulating hormone (FSH) and luteinizing hormone (LH) occur after 1 week of leuprolide treatment. There is a paradoxical stimulation of the release of LH and FSH initially during the first week of treatment.

3) ACID PHOSPHATASE SUPPRESSION: Significant decreases in acid phosphatase levels occur after 4 weeks of treatment, with most patients exhibiting decreases after 12 weeks of treatment.

B) Duration

1) Single Dose

a) A single dose of leuprolide acetate 11.25 mg effectively suppressed testosterone serum levels to castration range (less than 1.73 nmol/L) for at least 13 weeks.