Leuprorelin
A Review of its Pharmacology and Therapeutic Use in Prostatic Cancer, Endometriosis and Other Sex Hormone–Related Disorders

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Leuprorelin (leuprolide acetate) is a gonadotrophin-releasing hormone (GnRH) analogue used to treat a wide range of sex hormone–related disorders including advanced prostatic cancer, endometriosis and precocious puberty. It acts primarily on the anterior pituitary, inducing a transient early rise in gonadotrophin release. With continued use, leuprorelin causes pituitary desensitisation and/or down-regulation, leading to suppressed circulating levels of gonadotrophins and sex hormones.

Clinical trials in men with advanced prostatic cancer demonstrate that leuprorelin (usually monthly depot injections of 3.75 or 7.5mg) is less likely to cause serious adverse cardiovascular effects than diethylstilbestrol, and has comparable efficacy to bilateral orchiectomy or other GnRH analogues. Therefore, the choice between leuprorelin and orchiectomy may be made on the basis of the patient’s treatment preference, along with specific patient characteristics and cost implications.

Monthly intramuscular or subcutaneous administration of depot leuprorelin 3.75mg was superior to placebo, and comparable to oral danazol 800 mg/day or intranasal buserelin 900 µg/day, in achieving objective and subjective responses in women with endometriosis. Thus, leuprorelin is an effective alternative to other treatments for women with endometriosis, but the recommended duration of its use in this clinical setting is limited to 6 months because it reduces bone mineral density.

In children with central precocious puberty, leuprorelin (usually monthly intramuscular or subcutaneous injections of depot leuprorelin 3.75 to 15mg) decreases mean growth velocity and signs of sexual maturation and increases predicted adult height compared with baseline measurements. Although effects on final adult height are predicted from available data and require confirmation in long term follow-up studies, the absence of effective alternatives to GnRH analogues makes leuprorelin a first-line therapy for children with this rare disease.

In women with uterine leiomyomata, monthly intramuscular administration of depot leuprorelin 3.75mg for 6 months markedly reduces uterine volume and fibroid-related symptoms, but, as with other GnRH analogues, these effects dissipate following discontinuation of the drug. As adjuvant therapy in women undergoing in vitro fertilisation or gamete intrafallopian transfer, leuprorelin (usually 0.5 to 1 mg/day subcutaneously) reduces the risk of cancelled cycles for oocyte retrieval by preventing premature luteinisation. While some studies demonstrate an improvement in intermediate end-points such as increased number of mature oocytes retrieved and embryos available for transfer, a significant effect has not been demonstrated on the rate of live births per stimulated cycle.

The tolerability profile of leuprorelin varies somewhat depending on the patient’s gender and/or disease state because most adverse effects associated with leuprorelin result from changes in levels of circulating sex hormones. In men with prostatic cancer receiving leuprorelin, impotence and decreased libido occur almost universally, hot flushes are reported by 35 to 71% of men and exacerbation of symptoms (disease flare) occurs in approximately 10%. Hot flushes occur in approximately 80% of women receiving leuprorelin for endometriosis and other common adverse events include headache, vaginitis/vaginal dryness, insomnia and emotional lability. Children with precocious puberty appear to tolerate