

GONADOTROPIN-RELEASING HORMONES

Firmagon (degarelix), Supprelin LA (histrelin), Trelstar (triptorelin), Triptodur (triptorelin), (histrelin), Zoladex (goserelin)

RATIONALE FOR INCLUSION IN PA PROGRAM**Background**

Gonadotropin-releasing hormone (GnRH) analogs are used to suppress the pubertal hormones (1). Initial administration of GnRH analogs leads to an increase in circulating levels of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), leading to a transient increase in concentration of gonadal steroids (testosterone and dihydrotestosterone in males, and estrone and estradiol in premenopausal females) (2-5). After continuous chronic administration, GnRH analogs down-regulate the GnRH receptors in the pituitary gland and cause desensitization of the pituitary gonadotropes. This desensitization leads to a sustained decrease in LH and FSH secretion. In males, this results in testosterone levels equivalent to castration levels, and in females, this results in estradiol levels equivalent to a postmenopausal state (2-5). Slight development of sex characteristics will regress and, in a later phase of pubertal development, will be halted (1).

For use in Gender Dysphoria (GD), GnRH analogues work with cross-sex steroid therapy to maintain full suppression of pituitary gonadotropin levels and gonadal steroids. The actions of GnRH analogues are reversible upon cessation of treatment. Spontaneous pubertal development should resume shortly after GnRH treatment is discontinued (1).

Regulatory Status

The drugs addressed by this policy are FDA-approved for use in one or more of a variety of different conditions.

1. Supprelin LA (histrelin) – indicated for central precocious puberty in children and for the palliative treatment of advanced prostate cancer (2)
2. Trelstar (triptorelin) – indicated for the palliative treatment of advanced prostate cancer (4)
3. Vantas (histrelin) – indicated for central precocious puberty in children and for the palliative treatment of advanced prostate cancer (5)
4. Zoladex (goserelin) – indicated for use in combination with flutamide for the management of locally confined carcinoma of the prostate, palliative treatment of advanced carcinoma of the prostate, the management of endometriosis, use as an endometrial-thinning agent prior to endometrial ablation for dysfunction uterine bleeding, and use in the palliative treatment of advanced breast cancer in pre-and perimenopausal women (3)
5. Triptodur (triptorelin) – indicated for the treatment of pediatric patients 2 years and older with central precocious puberty (6)



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6. Firmagon (degarelix) indicated for treatment of patients with advanced prostate cancer (7)

Off Label Use:

GnRH analogues can be used in the treatment of Gender Dysphoria (GD) and should only be started once a diagnosis of GD or transsexualism has been made per the DSM V or ICD-10 criteria (1).

Summary

Gonadotropin-releasing hormone (GnRH) analogs are used to suppress the pubertal hormones (1). Initial administration of GnRH analogs leads to an increase in circulating levels of luteinizing hormone (LH) and follicle-stimulating hormone (FSH), leading to a transient increase in concentration of gonadal steroids (testosterone and dihydrotestosterone in males, and estrone and estradiol in premenopausal females). After continuous chronic administration, GnRH analogs down-regulate the GnRH receptors in the pituitary gland and cause desensitization of the pituitary gonadotropes (2-5). Gonadotropin-releasing hormone (GnRH) analogs are approved for a variety of conditions. GnRH analogs alter the regulation of the GnRH receptors in the pituitary gland. For a diagnosis of Gender Dysphoria (1).

Prior authorization is required to ensure the safe, clinically appropriate and cost effective use of drugs used for GD while maintaining optimal therapeutic outcomes.

References

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2. Supprelin LA [package insert]. Malvern, PA: Endo Pharmaceuticals Inc; April 2017.
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4. Trelstar [package insert]. Parsippany, NJ: Actavis Pharma, Inc; July 2014.
5. Vantas [package insert]. Malvern, PA: Endo Pharmaceuticals Inc; January 2014.
6. Triptodur [package insert]. Atlanta, GA: Arbor Pharmaceuticals, LLC; June 2017.
7. Firmagon [package insert]. Parsippany, NJ: Ferring Pharmaceuticals, Inc.; May 2017.