

## 5.30.39

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<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	April 1, 2021
<b>Subsection:</b>	Endocrine and Metabolic Drugs	<b>Original Policy Date:</b>	January 1, 2016
<b>Subject:</b>	GnRH Gender Dysphoria	<b>Page:</b>	1 of 5

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**Last Review Date:** March 12, 2021

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## GnRH Gender Dysphoria

### Description

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

### 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 decreased 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

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<b>Subject:</b>	GnRH Gender Dysphoria	<b>Page:</b>	2 of 5

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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)
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).

#### **Related policies**

ART Infertility, Synarel

#### **Policy**

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

The drugs listed may be considered **medically necessary** for all indications other than those that are considered to be Gender Dysphoria. Patients using these medications for Gender Dysphoria (GD) must meet the conditions indicated below.

<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	April 1, 2021
<b>Subsection:</b>	Endocrine and Metabolic Drugs	<b>Original Policy Date:</b>	January 1, 2016
<b>Subject:</b>	GnRH Gender Dysphoria	<b>Page:</b>	3 of 5

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## Prior-Approval Requirements

### Diagnoses

**ALL** diagnoses are covered **EXCEPT**:

For **Gender Dysphoria (GD)**:

**MUST HAVE ALL** of the following:

1. Prescribed by an endocrinologist or transgender specialist
2. Patient has met the DSM V criteria for GD

## Prior – Approval *Renewal* Requirements

### Diagnoses

**ALL** diagnoses are covered **EXCEPT**:

For **Gender Dysphoria (GD)**:

**MUST HAVE** the following:

1. Prescribed by an endocrinologist or transgender specialist

## Policy Guidelines

### Pre - PA Allowance

None

### Prior - Approval Limits

**Duration** 2 years

### Prior – Approval *Renewal* Limits

Same as above

## Rationale

### 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

<b>Section:</b>	Prescription Drugs	<b>Effective Date:</b>	April 1, 2021
<b>Subsection:</b>	Endocrine and Metabolic Drugs	<b>Original Policy Date:</b>	January 1, 2016
<b>Subject:</b>	GnRH Gender Dysphoria	<b>Page:</b>	4 of 5

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

1. Hembree, WC, Cohen-Kettenis, P, et al. Endocrine Treatment of Transsexual Persons: AA Endocrine Society Clinical Practice Guideline. The Journal of Clinical Endocrinology and Metabolism. 2009; 94(9):3132-3154
2. Supprelin LA [package insert]. Malvern, PA: Endo Pharmaceuticals, Inc.; November 2019.
3. Zoladex [package insert]. Lake Forest, IL: TerSera Therapeutics LLC; February 2019.
4. Trelstar [package insert]. Wayne, PA: Verity Pharmaceuticals Inc.; May 2020.
5. Vantas [package insert]. Malvern, PA: Endo Pharmaceuticals Inc; January 2014.
6. Triptodur [package insert]. Atlanta, GA: Arbor Pharmaceuticals, LLC; October 2018.
7. Firmagon [package insert]. Parsippany, NJ: Ferring Pharmaceuticals, Inc.; February 2020.

### Policy History

Date	Action
October 2015	Addition to PA
December 2015	Annual review
September 2016	Annual review
	Policy number change from 5.08.39 to 5.30.39
January 2017	Removal of GD age requirement and addition of transgender specialist
March 2017	Annual Review
August 2017	Addition of Triptodur
September 2017	Annual review
March 2018	Annual review
June 2018	Addition of Firmagon to criteria
September 2018	Annual review and reference update
December 2019	Annual editorial review and reference update. Changed approval duration from lifetime to 2 years
December 2020	Annual review and reference update
March 2021	Annual review

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<b>Subsection:</b>	Endocrine and Metabolic Drugs	<b>Original Policy Date:</b>	January 1, 2016
<b>Subject:</b>	GnRH Gender Dysphoria	<b>Page:</b>	5 of 5

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## Keywords

**This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 12, 2021 and is effective on April 1, 2021.**