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Section:	Prescription Drugs	**Effective Date:**	January 1, 2020
Subsection:	Endocrine and Metabolic Drugs	**Original Policy Date:**	January 1, 2016
Subject:	GnRH Gender Dysphoria	**Page:**	1 of 5

Last Review Date: December 6, 2019

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

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.

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

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.; May 2017.
3. Zoladex [package insert]. Lake Forest, IL: TerSera Therapeutics LLC; February 2019.
4. Trelstar [package insert]. Irvine, CA: Allergan USA, Inc.; December 2018.
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.; May 2017.

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

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 6, 2019 and is effective on January 1, 2020.