Effective Date **4/1/2023**
Next Review Date… **4/1/2024**
Coverage Policy Number **IP0133**

Histrelin Acetate Subcutaneous Implant

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Related Coverage Resources

Treatment of Gender Dysphoria

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This policy supports medical necessity review for the following histrelin acetate product(s):

- Supprelin LA® (histrelin acetate subcutaneous implant)

Receipt of sample product does not satisfy any criteria requirements for coverage.

Initial Approval Criteria

Histrelin acetate subcutaneous implant (Supprelin LA) is considered medically necessary for the treatment of central precocious puberty (CPP) when the individual meets ALL of the following criteria:

1. Onset of secondary sexual characteristics earlier than 8 years in females and 9 years in males
2. Documented diagnosis confirmed by **ONE** of the following:
    a. Pubertal basal level of luteinizing hormone (LH) greater than or equal to 0.3 mIU/ml

b. Pubertal luteinizing hormone (LH) response to a GnRH stimulation test

Dosing. The recommended dose is one implant (50 mg) once every 12 months (inserted subcutaneously in the upper arm).

Histrelin acetate subcutaneous implant (Supprelin LA) is considered medically necessary for the treatment of gender-dysphoric/gender-incongruent persons and/or persons undergoing gender reassignment (female-to-male or male-to-female) when the following criteria is met:

Medication is prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of transgender individuals

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When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Continuation of Therapy

Continuation of histrelin acetate subcutaneous implant (Supprelin LA) is considered medically necessary for **ALL** covered diagnoses when initial criteria are met AND beneficial response is demonstrated.

Authorization Duration

Initial approval duration is up to 12 months.
Reauthorization approval duration is up to 12 months.

Conditions Not Covered

Any other use is considered experimental, investigational or unproven including the following (this list may not be all inclusive):

Peripheral Precocious Puberty (also known as Gonadotropin-Releasing Hormone-independent precocious puberty). Children with peripheral precocious puberty do not respond to GnRH agonist therapy.[4] Treatment is directed at removing or blocking the production and/or response to the excess sex steroids, depending on the cause (e.g., surgically removing human chorionic gonadotropin-secreting tumors or using glucocorticoids to treat defects in adrenal steroidogenesis [such as classic congenital adrenal hyperplasia]).

Coding Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J9226	Histrelin implant (Supprelin la), 50 mg

Background

OVERVIEW
Supprelin LA is a gonadotropin-releasing hormone (GnRH) agonist implant.[1-4]

Supprelin LA is indicated for the treatment of children with **central precocious puberty**.[1]

Vantas is indicated for the palliative treatment of **advanced prostate cancer**.[2] Although Vantas is not indicated for use in children with central precocious puberty, it contains the same chemical entity as Supprelin LA and can be used for this condition. Endo made a business decision to discontinue manufacture of Vantas as of 9/21/2021.[6]

Guidelines
The GnRH agonists are addressed in treatment guidelines:

- **Central precocious puberty:** The European Society for Paediatric Endocrinology and the Lawson Wilkins Pediatric Endocrine Society convened a consensus conference (2009) to review the use of GnRH agonists in pediatric patients with central precocious puberty.[7] The panel noted that the available GnRH agonists (including leuprolide, triptorelin, and histrelin implant) are effective despite different routes of administration, dosing, and duration of action. An update by the International Consortium (2019) reiterates the use of GnRH agonists (e.g., leuprolide, triptorelin, and histrelin implant) for the treatment of central precocious puberty.[8]
- **Prostate cancer:** The NCCN prostate cancer guidelines (version 3.2022 – January 10, 2022) list both histrelin and goserelin as androgen deprivation therapy options for use in various settings (all category 2A): clinically localized disease, regional disease, prostate specific antigen persistence/recurrence after radical prostatectomy or external beam radiation therapy (castration-naïve disease), and metastatic castration-naïve disease.[9]

References

1. Supprelin® LA subcutaneous implant [prescribing information]. Malvern, PA: Endo Pharmaceuticals; November 2019.
2. Vantas® subcutaneous implant [prescribing information]. Malvern, PA: Endo Pharmaceuticals; December 2020.
3. Zoladex® 3.6 mg subcutaneous implant [prescribing information]. Lake Forest, IL: TerSera Therapeutics; December 2020.
4. Zoladex® 10.8 mg subcutaneous implant [prescribing information]. Lake Forest, IL: TerSera Therapeutics; December 2020.
5. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (version 2.2022 – December 20, 2021). © 2021 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on February 2, 2022.
6. FDA Drug Shortages. Current and resolved drug shortages and discontinuations reported to FDA. September 21, 2021. Available at: FDA Drug Shortages. Access on February 2, 2022.
7. Carel JC, Eugster EA, Rogol A, et al. Consensus statement on the use of gonadotropin-releasing hormone analogs in children. *Pediatrics*. 2009 Apr;123(4):e752-62.
8. Krishna KB, Fuqua JS, Rogol AD, et al. Use of gonadotropin-releasing hormone analogs in children: update by an international consortium. *Horm Res Paediatr*. 2019;91:357-372.
9. The NCCN Prostate Cancer Clinical Practice Guidelines in Oncology (version3.2022 – January 10, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org/. Accessed on February 2, 2022.