Drug Coverage Policy

Effective Date 01/01/2025
Coverage Policy Number.....IP0620
Policy Title.....Gonadotropin-Releasing Hormone Agonists – Implants for Non-Oncology Indications

Gonadotropin-Releasing Hormone Agonists – Implants for Non-Oncology Indications

- Supprelin® LA (histrelin acetate subcutaneous implant – Endo)
- Zoladex® (goserelin acetate subcutaneous implant – TerSera Therapeutics)

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. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment and have discretion in making individual coverage determinations. 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.

Cigna Healthcare Coverage Policy

OVERVIEW
Supprelin LA and Zoladex are gonadotropin-releasing hormone (GnRH) agonists implants.[1-4]

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

Zoladex is indicated for the following conditions:[3,4] Zoladex 3.6 mg (equivalent to 3.8 mg goserelin acetate) is approved for all the diagnoses below. Zoladex 10.8 mg (equivalent to 11.3 mg goserelin acetate) is only indicated for prostate cancer.

- **Breast cancer**, palliative treatment of advanced breast cancer in pre- and perimenopausal women (Zoladex 3.6 mg implant only).
- **Endometrial-thinning**, use as an endometrial-thinning agent prior to endometrial ablation for dysfunctional uterine bleeding (Zoladex 3.6 mg implant only).
- **Endometriosis**, including pain relief and reduction of endometriotic lesions for the duration of therapy (Zoladex 3.6 mg implant only). Labeling notes that experience with Zoladex for this indication has been limited to women ≥ 18 years of age.[3]
- **Prostate cancer**, in combination with flutamide for the management of locally confined Stage T2b-T4 (Stage B2-C).
- **Prostate cancer**, advanced carcinoma, or palliative treatment.

Guidelines

The GnRH agonists are addressed in treatment guidelines:

- **Central precocious puberty**, also known as gonadotropin-dependent precocious puberty, is caused by early maturation of the hypothalamic-pituitary-gonadal axis.[5] The standard of care for central precocious puberty is GnRH agonists. 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 implants) 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 implants) for the treatment of central precocious puberty.[7] GnRH agonists are generally well-tolerated in children and adolescents.

Medical Necessity Criteria

Coverage for the use of goserelin acetate subcutaneous implant (Zoladex) and histrelin acetate subcutaneous implant for oncology indications is addressed in a separate coverage policy.

Coverage for treatment of gender dysphoria varies across plans. Coverage of drugs for hormonal therapy, as well as whether the drug is covered as a medical or a pharmacy benefit, varies across plans. Refer to the customer's benefit plan document for coverage details. In addition, coverage for treatment of gender dysphoria, including gender reassignment surgery and related services may be governed by state and/or federal mandates.

I. Supprelin LA is considered medically necessary when the following is met:

FDA-Approved Indication

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1. Central Precocious Puberty. Approve for 1 year if the patient meets the following (A, B, and C):

A) Pubertal basal level of luteinizing hormone (LH) greater than or equal to 0.2 mIU/ml
B) Pubertal luteinizing hormone (LH) response to a GnRH agonist stimulation test
C) Preferred product criteria is met for the product as listed in the below tables - **Central Precocious Puberty (CPP)**

Dosing. Approve one implant (50 mg) once every 12 months (inserted subcutaneously in the upper arm).

Other Uses with Supportive Evidence

2. Gender-Dysphoric/ Gender-Incongruent Persons; Persons Undergoing Gender Reassignment (Female-to-Male or Male-to-Female). Approve for 1 year if prescribed by or in consultation with an endocrinologist or a physician who specializes in treatment of transgender patients.

Employer Plans:

Product	Criteria
Supprelin LA (histrelin acetate subcutaneous implant)	**Central Precocious Puberty (CPP)** Patient meets at least **ONE** of the following (i or ii): i. Patient has tried ONE of Fensolvi or Triptodur; OR ii. Patient is < 2 years of age.

Individual and Family Plans:

Product	Criteria
Supprelin LA (histrelin acetate subcutaneous implant)	**Central Precocious Puberty (CPP)** Patient meets at least **ONE** of the following (i or ii): i. Patient has tried ONE of Fensolvi or Triptodur; OR ii. Patient is < 2 years of age.

II. Zoladex is considered medically necessary when the following are met:

FDA-Approved Indications

1. **Abnormal Uterine Bleeding.** Approve for 2 months if the patient meets the following (A and B):
   A) Zoladex is used as an endometrial-thinning agent prior to endometrial ablation; AND
   B) The medication is prescribed by or in consultation with an obstetrician-gynecologist or a health care practitioner who specializes in the treatment of women's health.

   Dosing. Approve Zoladex 3.6 mg implant once every 28 days (inserted subcutaneously into the anterior abdominal wall).

2. **Endometriosis.** Approve for 6 months if the patient meets the following (A and B):
   A) Patient is ≥ 18 years of age; AND
   B) The medication is prescribed by or in consultation with an obstetrician-gynecologist or a health care practitioner who specializes in the treatment of women's health.

   Dosing. Approve Zoladex 3.6 mg implant once every 28 days (inserted subcutaneously into the anterior abdominal wall).

Other Uses with Supportive Evidence

3. **Gender-Dysphoric/Gender-Incongruent Persons; Persons Undergoing Gender Reassignment (Female-To-Male or Male-To-Female.** Approve for 1 year if prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of transgender patients

4. **Preservation of Ovarian Function/Fertility in Patients undergoing Chemotherapy.** Approve Zoladex for 1 year if prescribed by or in consultation with an obstetrician-gynecologist or an oncologist.

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.

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

Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

1. **Peripheral Precocious Puberty (also known as GnRH-independent precocious puberty)**.Children with peripheral precocious puberty do not respond to GnRH agonist therapy.[7] 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

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
J9202	Goserelin acetate implant, per 3.6 mg
J9226	Histrelin implant (Supprelin LA), 50 mg

References

1. Supprelin® LA [prescribing information]. Malvern, PA: Endo; April 2022.
2. Vantas® subcutaneous implant [prescribing information]. Malvern, PA: Endo; February 2022.
3. Zoladex® 3.6 mg implant [prescribing information]. Lake Forest, IL: TerSera Therapeutics; March 2023.
4. Zoladex® 10.8 mg implant [prescribing information]. Lake Forest, IL: TerSera Therapeutics; December 2020.
5. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (version 1.2024 – January 25, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 6, 2024.
6. Eugster EA. Treatment of central precocious puberty. J Endo Soc. 2019;3:965-972.
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 (version 4.2023 – September 7, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 6, 2024.
10. American Society of Health System Pharmacists (ASHP). ASHP current drug shortages. September 24, 2021. Available at: Drug Shortage Detail: Histrelin Implant (ashp.org). Access on February 6, 2024.
11. The NCCN Drugs and Biologics Compendium. 2024 © National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 6, 2024. Search term: Zoladex.
12. The NCCN Uterine Neoplasms Clinical Practice Guidelines in Oncology (version 1.2024 – September 20, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 6, 2024.
13. The NCCN Head and Neck Cancers Clinical Practice Guidelines in Oncology (version 2.2024 – December 08, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 6, 2024.
14. The NCCN Ovarian Cancer Clinical Practice Guidelines in Oncology (version 1.2024 – January 17, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 6, 2024.

Revision Details

Type of Revision	Summary of Changes	Date
Annual Revision	**Removed** histrelin acetate medical necessity criteria which defines for use relating to *Central Precocious Puberty* (onset of secondary sexual characteristics).	6/1/2024
Selected Revision	**Added** preferred product requirement criteria for patients with central precocious puberty for employer plans and individual and family plans.	01/01/2025

The policy effective date is in force until updated or retired.