Effective Date **8/1/2023**
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Coverage Policy Number **IP0353**

Goserelin Acetate Subcutaneous Implant

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Oncology Medications
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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 goserelin acetate subcutaneous implant (**Zoladex®**).

Note: The use of goserelin acetate subcutaneous implant (Zoladex) for oncology indications is addressed in a separate coverage policy. Please refer to the related coverage policy link above (Oncology Medications).

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[14]

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

Medical Necessity Criteria

Goserelin acetate subcutaneous implant (Zoladex) is considered medically necessary when ONE of the following is met (1, 2, 3, or 4):

1. **Abnormal Uterine Bleeding.** Individual meets **BOTH** of the following criteria (A and B):
   A. Zoladex is used as an endometrial-thinning agent prior to endometrial ablation
   B. Medication is prescribed by or in consultation with an obstetrician-gynecologist

2. **Endometriosis.** Individual meets **BOTH** of the following criteria (A and B):
   A. Individual is 18 years of age or older
   B. Medication is prescribed by or in consultation with an obstetrician-gynecologist

3. **Gender-Dysphoric/Gender-Incongruent Persons; Persons Undergoing Gender Reassignment (Female-To-Male or Male-To-Female).** Individual meets the following criteria:
   A. Medication is prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of transgender patients

4. **Prevention of Early Menopause During Chemotherapy for Hormone Receptor-Negative Breast Cancer.** Individual meets **BOTH** of the following criteria (A and B):
   A. Individual is premenopausal or perimenopausal
   B. Medication is 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.

Reauthorization Criteria

Goserelin acetate subcutaneous implant (Zoladex) is considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration:

- Abnormal Uterine Bleeding: up to 2 months
- Endometriosis: up to 6 months
- Gender-Dysphoric/Gender-Incongruent Persons; Persons Undergoing Gender Reassignment (Female-To-Male or Male-To-Female): up to 12 months
- Prevention of early menopause during chemotherapy for hormone receptor-negative breast cancer: up to 12 months

Reauthorization approval duration:

- Abnormal Uterine Bleeding: Not applicable for continuation beyond initial approval duration.
- Endometriosis: Not applicable for continuation beyond initial approval duration.
- Gender-Dysphoric/Gender-Incongruent Persons; Persons Undergoing Gender Reassignment (Female-To-Male or Male-To-Female): up to 12 months
- Prevention of early menopause during chemotherapy for hormone receptor-negative breast cancer: up to 12 months

Conditions Not Covered

Goserelin acetate subcutaneous implant (Zoladex) is considered experimental, investigational or unproven for **ANY** other use including the following (this list may not be all inclusive):

1. **Peripheral Precocious Puberty (also known as GnRH-independent precocious puberty).** Children with peripheral precocious puberty do not respond to GnRH agonist therapy.[8] 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
J9202	Goserelin acetate implant, per 3.6 mg

Background

OVERVIEW
Zoladex is a gonadotropin-releasing hormone (GnRH) agonist implant.[3,4]

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).
- **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:

- **Breast cancer:** The National Comprehensive Cancer Network (NCCN) breast cancer guidelines (version 1.2023 – January 27, 2023) do not note the use of Zoladex implants for advanced breast cancer.[5] However, the guidelines note that GnRH agonists (e.g., goserelin) administered prior to initiating chemotherapy protect against ovarian failure and reduce the risk of early menopause. Ovarian suppression may be recommended in patients who are premenopausal at diagnosis.
- **Central precocious puberty**, also known as gonadotropin-dependent precocious puberty, is caused by early maturation of the hypothalamic-pituitary-gonadal axis.[6] 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 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] GnRH agonists are generally well-tolerated in children and adolescents.

- **Prostate cancer:** The NCCN prostate cancer guidelines (version 1.2023 – September 16, 2022) list goserelin, leuprolide, and triptorelin as androgen deprivation therapy options for use in various settings: clinically localized disease, regional disease, prostate specific antigen persistence/recurrence after radical prostatectomy or external beam radiation therapy (castration-sensitive disease), and metastatic castration-sensitive disease.[9]

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; December 2020.
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 1.2023 – January 27, 2023). © 2023 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 2, 2023.
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 1.2023 – September 16, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 2, 2023.
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 2, 2023.