UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Gonadotropin-Releasing Hormone Agonists – Implants Utilization Management Medical Policy
- Supprelin® LA (histrelin acetate subcutaneous implant – Endo)
- Zoladex® (goserelin acetate subcutaneous implant – TerSera Therapeutics)

REVIEW DATE: 02/11/2026; selected revision 04/01/2026 and 09/09/2026

OVERVIEW

Supprelin LA and Zoladex are gonadotropin-releasing hormone (GnRH) agonists implants.[1-3]

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

Zoladex is indicated for the following conditions:[2,3]
- **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.[2]
- **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.

Zoladex 3.6 mg (equivalent to 3.8 mg goserelin acetate) is approved for all the diagnoses above. Zoladex 10.8 mg (equivalent to 11.3 mg goserelin acetate) is only indicated for prostate cancer.

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.[6] 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.

Endometrosis: Care pathways available from American Family Physician (2022) recommend estrogen-progestin combination products or progestins as first-line medical therapies for endometriosis.[21] Second-line treatment consists of GnRH receptor agonists or antagonists. Aromatase inhibitors are reserved for severe disease.

Gender-dysphoric/gender-incongruent persosns: According to the Endocrine Society Guidelines for the treatment of gender dysphoric/gender-incongruent persons and the World Professional Association for Transgender Health, GnRH agonists can be used off-label for the treatment of gender-dysphoric/gender-

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incongruent persons to suppress physical changes of puberty and gonadal function.[17,18] Pubertal hormonal suppression should typically be initiated after the adolescent first exhibits physical changes of puberty (Tanner stages G2/B2). An advantage to using a GnRH analog is that the effects can be reversed; pubertal suppression can be discontinued if the individual no longer wishes to transition. Upon discontinuation of therapy, spontaneous pubertal development has been shown to resume. GnRH analogs can also be used in patients during late puberty to suppress the hypothalamic-pituitary-gonadal axis to allow for lower doses of cross-sex hormones.[19] In addition to use in adolescents, GnRH analog therapy is also used in adults, particularly male-to-female patients.[13]

In addition to the approved indications, GnRH agonists have been used for other conditions. The National Comprehensive Cancer Network (NCCN) guidelines address the use of GnRH agonists in a number of guidelines:

- **Adolescent and young adult oncology** NCCN guidelines (version 2.2026 – February 27, 2026) note GnRH agonists may be used in (oncology) protocols that are predicted to cause prolonged thrombocytopenia and present a risk for menorrhagia.[20] There are some limited data on GnRH agonists to preserve ovarian function during chemotherapy and some have shown that GnRH agonists may be beneficial for fertility preservation, although the guidelines note further investigation is needed and other fertility preservation modalities should still be pursued.
- **Breast cancer:** The NCCN breast cancer guidelines (version 1.2026 – January 16, 2026) note methods for ovarian function suppression in breast cancer includes goserelin 3.6 mg subcutaneous every 4 weeks or 10.8 mg subcutaneous every 12 weeks.[4] Other previous information from NCCN regarding goserelin in breast cancer is under discussion.
- **Head and neck cancer – salivary gland tumors:** The NCCN head and neck cancer guidelines (version 1.2026 – December 8, 2025) notes that goserelin (category 2B) is useful for androgen receptor positive salivary gland tumors which are recurrent, unresectable, or metastatic.[9,11] Goserelin can also be used (category 2A) with abiraterone and prednisone. Dosing used in NCCN references was 3.6 mg subcutaneously once every 28 days.[14-16]
- **Ovarian cancer, including fallopian tube cancer and primary peritoneal cancer:** The NCCN ovarian cancer guidelines (version 3.2025 – July 16, 2025) notes goserelin as other hormone therapy options for endometrioid carcinoma, low-grade serous carcinoma, malignant sex cord stromal tumors (for granulosa cell tumors), and recurrence therapy for platinum-sensitive disease.[9,12] Goserelin is an option for hormonal therapy.
- **Prostate cancer:** The NCCN prostate cancer guidelines (version 5.2026 – January 23, 2026) list goserelin, leuprolide, and triptorelin as androgen deprivation therapy options for use in various settings: clinically localized disease, regional disease, positive lymph nodes and/or adverse features post-radical prostatectomy, first persistence/recurrence, castration-sensitive disease, metastatic castration-sensitive disease, and castration-resistant disease.[8]
- **Uterine cancer:** The NCCN uterine neoplasm guidelines (version 2.2026 – November 14, 2025) notes that prescribers may consider GnRH analogs with aromatase inhibitors in patients who are premenopausal and not suitable for surgery for low-grade endometrial stromal sarcoma, adenosarcoma without sarcomatous overgrowth, or hormone receptor-positive uterine sarcomas.[9,10]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Supprelin LA and Zoladex. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required

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for evaluation and diagnosis of patients treated with Zoladex as well as the monitoring required for adverse events and long-term efficacy, approval requires these agents to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

I. Coverage of Supprelin LA is recommended in patients who meet the following criteria:

FDA-Approved Indication

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1. Central Precocious Puberty. Approve for 1 year.

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 [FTM] or Male-to-Female [MTF]). Approve for 1 year if prescribed by or in consultation with an endocrinologist or a physician who specializes in the treatment of transgender patients**.**

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

II. Coverage of Zoladex is recommended in patients who meet one of the following criteria:

FDA-Approved Indications

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1. Abnormal Uterine Bleeding. Approve for 2 months if the patient meets BOTH of 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).

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2. Breast Cancer. . Approve for 1 year if the medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosage regimens (inserted subcutaneously into the anterior abdominal wall) [A or B]:
- **A)** Zoladex 3.6 mg implant once every 28 days; OR
- **B)** Zoladex 10.8 mg implant once every 12 weeks.

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3. Endometriosis. Approve for 6 months if the patient meets ALL of the following (A, B, and C):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has tried at least ONE of the following, unless contraindicated (i, ii, or iii):
  - **i.** A contraceptive (e.g., combination oral contraceptive, levonorgestrel-releasing intrauterine systems [e.g., Mirena, Liletta]); OR
  - **ii.** An oral progesterone (e.g., norethindrone tablets); OR
  - **iii.** A depo-medroxyprogesterone injection; AND

  Note: An exception to the requirement for a trial of the above therapies can be made if the patient has previously used a gonadotropin-releasing hormone (GnRH) agonist (e.g., Lupron Depot) or antagonist (e.g., Orilissa).
- **C)** 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).

4. Prostate Cancer. . Approve for 1 year if the medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following dosage regimens (inserted subcutaneously into the anterior abdominal wall) [A or B]:
- **A)** Zoladex 3.6 mg implant once every 28 days; OR
- **B)** Zoladex 10.8 mg implant once every 12 weeks.

Other Uses with Supportive Evidence

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

Dosing. Approve ONE of the following dosage regimens (inserted subcutaneously into the anterior abdominal wall) [A or B]:
- **A)** Zoladex 3.6 mg implant once every 28 days; OR
- **B)** Zoladex 10.8 mg implant once every 12 weeks.

6. Head and Neck Cancer – Salivary Gland Tumors. . Approve for 1 year if the patient meets ALL of the following (A, B, and C):
- **A)** Patient has recurrent, unresectable, or metastatic disease; AND
- **B)** Patient has androgen receptor-positive disease; AND
- **C)** The medication is prescribed by or in consultation with an oncologist.

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

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7. **Ovarian Cancer, including Fallopian Tube Cancer and Primary Peritoneal Cancer**. . Approve for 1 year if the medication is prescribed by or in consultation with an oncologist.

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

8. **Preservation of Ovarian Function/Fertility in Patients Undergoing Chemotherapy**. . Approve for 1 year if the medication is prescribed by or in consultation with an obstetrician-gynecologist or an oncologist.

   Dosing. Approve ONE of the following dosage regimens (inserted subcutaneously into the anterior abdominal wall) [A or B]:
   A) Zoladex 3.6 mg implant once every 28 days; OR
   B) Zoladex 10.8 mg implant once every 12 weeks.

9. **Prophylaxis or Treatment of Uterine Bleeding or Menstrual Suppression in Patients with Hematologic Malignancy, or Undergoing Cancer Treatment, or Prior to Bone Marrow/Stem Cell Transplantation**. . Approve for 1 year if the medication is prescribed by or in consultation with an oncologist.

   Dosing. Approve ONE of the following dosage regimens (inserted subcutaneously into the anterior abdominal wall) [A or B]:
   A) Zoladex 3.6 mg implant once every 28 days; OR
   B) Zoladex 10.8 mg implant once every 12 weeks.

10. **Uterine Cancer**. . Approve for 1 year if the medication is prescribed by or in consultation with an oncologist.

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

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Supprelin LA and Zoladex is not recommended in the following situations:

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]).

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	02/15/2023
Annual Revision	**Head and Neck Cancer – Salivary Gland Tumors; Ovarian Cancer, including Fallopian Tube Cancer and Primary Peritoneal Cancer; Uterine Cancer.** These new conditions and criteria were added to the policy. **Breast Cancer:** Removal of criteria related to premenopausal or perimenopausal women. Added the following dosing regimen for approval: Zoladex 10.8 mg every 12 weeks.	02/21/2024
Annual Revision	Removed Vantas from the policy (obsolete).	02/12/2025
Annual Revision	**Other Uses with Supportive Evidence:** Gender-Dysphoric/Gender-Incongruent Persons; Persons Undergoing Gender Reassignment (Female-To-Male or Male-To-Female) was added as a new condition of approval for Supprelin LA and Zoladex.	02/11/2026
Selected Revision	**Preservation of Ovarian Function/Fertility in Patients Undergoing Chemotherapy; Prophylaxis or Treatment of Uterine Bleeding or Menstrual Suppression in Patients with Hematologic Malignancy, or Undergoing Cancer Treatment, or Prior to Bone Marrow/Stem Cell Transplantation:** These conditions of approval were added to the policy for Zoladex.	04/01/2026

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Selected Revision	**Enometriosis:** Added a criterion requiring a trial of a contraceptive, an oral progesterone, or a depo-medroxyprogesterone injection, unless contraindicated. A note was also added noting that an exception can be provided if the patient has previously used a gonadotropin-releasing hormone agonist or antagonist.	09/09/2026

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