PRIOR AUTHORIZATION POLICY

POLICY: Gonadotropin-Releasing Hormone Agonists – Implants Prior Authorization Policy
- Supprelin® LA (histrelin acetate subcutaneous implant – Endo)
- Vantas® (histrelin acetate subcutaneous implant – Endo [discontinued])
- Zoladex® (goserelin acetate subcutaneous implant – TerSera Therapeutics)

REVIEW DATE: 02/21/2024

OVERVIEW

Supprelin LA, Vantas, and Zoladex are gonadotropin-releasing hormone (GnRH) agonist implants.[1-4]

Supprelin LA is indicated for the treatment of **central precocious puberty** in children.[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 discontinued the manufacturing of Vantas as of 9/21/2021.[10]

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:

- **Breast cancer:** The National Comprehensive Cancer Network (NCCN) breast cancer guidelines (version 1.2024 – January 25, 2024) note that candidates for ovarian suppression plus endocrine therapy include: 1) premenopausal women, and 2) endocrine sensitive tumors with high enough recurrence risk where the additional absolute decrease in recurrence compared with tamoxifen alone is worth the additional toxicity (young age, high-grade tumor, lymph node involvement).[5] Goserelin doses for breast cancer are recommended at 3.6 mg subcutaneous every 4 weeks or 10.8 mg subcutaneous every 12 weeks. Guidelines also 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 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.[8] GnRH agonists are generally well-tolerated in children and adolescents.

- **Head and neck cancer – salivary gland tumors:** The NCCN head and neck cancer guidelines (version 2.2024 – December 08, 2023) notes that goserelin (category 2B) is useful for androgen receptor positive salivary gland tumors which are recurrent, unresectable, or metastatic.[11,13]
- **Ovarian cancer, including fallopian tube cancer and primary peritoneal cancer:** The NCCN ovarian cancer guidelines (version 1.2024 – January 17, 2024) notes goserelin as other hormone therapy options for endometrioid carcinoma, low-grade serous carcinoma, and malignant sex cord stromal tumors.[11,14]
- **Prostate cancer:** The NCCN prostate cancer guidelines (version 4.2023 – September 7, 2023) 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]
- **Uterine cancer:** The NCCN uterine neoplasm guidelines (version 1.2024 – September 20, 2023) notes that GnRH analogs are included as a category 2B option for endometrial stromal sarcoma, adenosarcoma without sarcomatous overgrowth, and estrogen receptor-progesterone receptor positive uterine sarcomas.[11,12]

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Supprelin LA, Vantas, and Zoladex. 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 for evaluation and diagnosis of patients treated with Vantas and 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. Note that as with Supprelin LA, when Vantas is prescribed for central precocious puberty, it does not need to be prescribed by or in consultation with a specialist.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indication

1. Central Precocious Puberty. Approve for 1 year.

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

FDA-Approved Indication

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

Other Uses with Supportive Evidence

2. **Central Precocious Puberty.** Approve for 1 year.

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

FDA-Approved Indications

1. **Abnormal Uterine Bleeding.** Approve Zoladex 3.6 mg 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 healthcare practitioner who specializes in the treatment of women's health.

2. **Breast Cancer**. Approve Zoladex 3.6 mg or 10.8 mg for 1 year if the medication is prescribed by or in consultation with an oncologist.

3. **Endometriosis.** Approve Zoladex 3.6 mg 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 healthcare practitioner who specializes in the treatment of women's health.

4. **Head and Neck Cancer – Salivary Gland Tumors.** Approve Zoladex 3.6 mg for 1 year if the patient meets 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.

5. **Ovarian Cancer, including Fallopian Tube Cancer and Primary Peritoneal Cancer.** Approve Zoladex 3.6 mg for 1 year if the medication is prescribed by or in consultation with an oncologist.

6. **Prostate Cancer**. Approve Zoladex 3.6 mg or 10.8 mg for 1 year if the medication is prescribed by or in consultation with an oncologist.

7. **Uterine Cancer.** Approve Zoladex 3.6 mg for 1 year if the medication is prescribed by or in consultation with an oncologist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL
Coverage of Supprelin LA, Vantas, 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.[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]).

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

REFERENCES

1. Supprelin® LA subcutaneous implant [prescribing information]. Malvern, PA: Endo; April 2022.
2. Vantas® subcutaneous implant [prescribing information]. Malvern, PA: Endo; February 2022.
3. Zoladex® 3.6 mg subcutaneous implant [prescribing information]. Lake Forest, IL: TerSera Therapeutics; March 2023.
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 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.