Medicare Advantage Medical Utilization Review Policy

Policy:	**Gonadotropin-Releasing Hormone Agonists Implants Utilization Management Medical Policy** • Supprelin® LA (histrelin acetate subcutaneous implant – Endo Pharmaceuticals) • Vantas® (histrelin acetate subcutaneous implant – Endo Pharmaceuticals [discontinued]) • Zoladex® (goserelin acetate subcutaneous implant – TerSera Therapeutics)
Date:	02/28/2022
Applicable Lines of Business:	Medicare Advantage - Medical
Applicable States:	NGS, J6: Wisconsin, Minnesota, Illinois NGS, JK: New York, Connecticut, Massachusetts, Maine, New Hampshire, Rhode Island, Vermont

Note: Supprelin LA is not addressed in Local Coverage Article A52453 or Local Coverage Determination L33394.[11-12]

OVERVIEW

Supprelin LA, Vantas, and Zoladex are gonadotropin-releasing hormone (GnRH) agonists implants.[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 that of Supprelin LA, and can be used for this condition. Endo made a business decision to discontinue manufacture 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).
- **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 2.2022 – December 20, 2021) does 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.
- **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 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]

POLICY STATEMENT

Prior authorization is recommended for medical benefit coverage of Supprelin LA, Vantas, and Zoladex. Approval is recommended for those who meet the Criteria and Dosing for the listed indication(s). Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. All approvals are provided for the duration noted below.

This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the References section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Reference section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage.

Note: Conditions for coverage outlined in this Medicare Advantage Medical Policy may be less restrictive than those found in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles. Examples of situations where this clinical policy may be less restrictive include, but are not limited to, coverage of additional indications supported by CMS-approved compendia and the exclusion from this policy of additional coverage criteria requirements outlined in applicable National Coverage Determinations, Local Coverage Determinations and/or Local Coverage Articles.

RECOMMENDED AUTHORIZATION CRITERIA

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

FDA-Approved Indications

1. Prostate Cancer.

Criteria. Approve for 1 year.

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

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

FDA-Approved Indications

1. Central Precocious Puberty.

Criteria. Approve for 1 year.

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

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

FDA-Approved Indications

1. Prostate Cancer.

Criteria. Approve for 1 year.

Dosing. Approve one implant (3.6 mg or 10.8 mg) 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.

2. Breast Cancer.

Criteria. Approve for 1 year if Zoladex is used in premenopausal or perimenopausal women.

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

3. Endometriosis.

Criteria. Approve for 6 months if the patient is ≥ 18 years of age.

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

4. Abnormal Uterine Bleeding.

Criteria. Approve for 2 months if Zoladex is used as an endometrial-thinning agent prior to endometrial abalation.

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

Other Uses with Supportive Evidence

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5. Uterine Leiomyomata (Fibroids).

Criteria. Approve for 6 months.

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, 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. 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 Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Supprelin® LA [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 implant [prescribing information]. Lake Forest, IL; December 2020.
4. Zoladex® 10.8 mg implant [prescribing information]. Lake Forest, IL; 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. 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 3.2022 – January 10, 2022). © 2022 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 2, 2022.
10. 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.

11. Centers for Medicare and Medicaid Services, National Government Services, Inc, Local Coverage Article: Luteinizing Hormone-Releasing Hormone (LHRH) Analogs – Related to LCD L33394 (A52453) (Original Effective Date 10/1/15, Revision Effective Date 05/01/2020). Accessed on February 28, 2022.

12. Centers for Medicare and Medicaid Services, National Government Services, Inc, Local Coverage Determination (LCD): Drugs and Biologicals, Coverage of, for Label and Off-Label Uses (L33394) [original date 10/01/2015; revision effective date 01/01/2022]. Accessed on February 28, 2022.

HISTORY

Type of Revision	Summary of Changes*	Date
Policy created	New policy created containing all LHRH products, see archived policy	7/11/18
Policy revision	Reviewed and revised original policy created 07/11/2018 in accordance with Local Coverage Article A52453.	8/28/2019
Policy revision	Reviewed and revised original policy created 07/11/2018 in accordance with Local Coverage Article A52453.	9/18/2019
Policy revision	Completion of 2019 monthly monitoring process in accordance with Local Coverage Determination L33394 and Local Coverage Article A52453.	11/25/2019
Policy revision	Non-clinical update to policy to add the statement "This policy incorporates Medicare coverage guidance as set forth in National Coverage Determinations (NCDs) and Local Coverage Determinations (LCDs), as well as in companion policy articles and other guidance applicable to the relevant service areas. These documents are cited in the References section of this policy. In some cases, this guidance includes specific lists of HCPCS and ICD-10 codes to help inform the coverage determination process. The Articles that include specific lists for billing and coding purposes will be included in the Reference section of this policy. However, to the extent that this policy cites such lists of HCPCS and ICD-10 codes, they should be used for reference purposes only. The presence of a specific HCPCS or ICD-10 code in a chart or companion article to an LCD is not by itself sufficient to approve coverage. Similarly, the absence of such a code does not necessarily mean that the applicable condition or diagnosis is excluded from coverage."	1/30/2020
Policy revision	*updated wording on dosing for all Zoladex indications to include "up to"	07/15/2020
Policy revision	No Criteria Changes	01/29/2021
Policy revision	Removal of the wording "up to" in all dosing sections.	02/28/2022