Clinical Policy: Histrelin Acetate (Vantas, Supprelin LA)

Reference Number: ERX.SPA.146
Effective Date: 10.01.16
Last Review Date: 11.21
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Histrelin acetate (Supprelin® LA, Vantas®) is a gonadotropin-releasing hormone (GnRH) agonist.

FDA Approved Indication(s)
Supprelin LA is indicated for the treatment of children with central precocious puberty (CPP).

Vantas is indicated for the palliative treatment of advanced prostate cancer.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Supprelin LA and Vantas are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Prostate Cancer (must meet all)**:**

1. Diagnosis of prostate cancer;
2. Request is for Vantas;
3. Prescribed by or in consultation with an oncologist or urologist;
4. Age ≥ 18 years;
5. Member must use all of the following, unless clinically significant adverse effects are experienced or all are contraindicated: leuprolide acetate injection (generic), Eligard®, Lupron® Depot (7.5 mg, 22.5 mg, 30 mg, or 45 mg);*
   **Prior authorization may be required for these agents*
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 50 mg per 12 months (one implant per year);
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).
   **Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Central Precocious Puberty (must meet all)**:**

1. Diagnosis of CPP confirmed by all of the following (a, b, and c):
   a. Elevated basal luteinizing hormone (LH) level > 0.2 - 0.3 mIU/L (dependent on type of assay used) and/or elevated leuprolide-stimulated LH level > 3.3 - 5 IU/L (dependent on type of assay used);
   b. Difference between bone age and chronological age was > 1 year (bone age-chronological age);
   c. Age at onset of secondary sex characteristics is < 8 years if female, or < 9 years if male;
2. Request is for Supprelin LA;
3. Prescribed by or in consultation with a pediatric endocrinologist;
4. Member meets one of the following age requirements (a or b):

a. Female: 2 to 11 years;
b. Male: 2 to 12 years;

5. Dose does not exceed 50 mg per 12 months (one implant per year).

Approval duration: 12 months

C. Other diagnoses/indications

1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Prostate Cancer (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Vantas for prostate cancer and has received this medication for at least 30 days;
2. Request is for Vantas;
3. Member is responding positively to therapy;
4. Request meets one of the following (a or b):*
   a. New dose does not exceed 50 mg per 12 months (one implant per year);
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN*

Approval duration: 12 months

B. Central Precocious Puberty (must meet all)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions or member has previously met initial approval criteria;
1. Request is for Supprelin LA;
2. Member is responding positively to therapy as evidenced by, including but not limited to, improvement in <u>any</u> of the following parameters: decreased growth velocity, cessation of menses, softening of breast tissue or testes, arrested pubertal progression;
3. Member meets one of the following age requirements (a or b):
   a. Female: ≤ 11 years;
   b. Male: ≤ 12 years;
4. If request is for a dose increase, new dose does not exceed 50 mg per 12 months (one implant per year).

Approval duration: 12 months

C. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CPP: central precocious puberty
FDA: Food and Drug Administration
GnRH: gonadotropin-releasing hormone
LH: luteinizing hormone
NCCN: National Comprehensive Cancer Network

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
leuprolide acetate injection (generic)	Prostate Cancer - Palliative Therapy SC: 1 mg per day	1 mg per day
Lupron Depot® 7.5, 22.5, 30, 45 (leuprolide acetate)	Prostate Cancer - Palliative Therapy IM: 7.5 mg per 4 weeks, 22.5 mg per 12 weeks, 30 mg per 16 weeks, or 45 mg per 24 weeks	See regimen
Eligard® (leuprolide acetate)	Prostate Cancer - Palliative Therapy SC: 7.5 mg per month, 22.5 mg per 3 months, 30 mg per 4 months, or 45 mg per 6 months	See regimen

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): hypersensitivity to GnRH, GnRH agonist analogs; pregnancy
- Boxed warning(s): none reported

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Histrelin acetate (Supprelin LA)	CPP	1 implant (50 mg) SC for 12 months	1 implant/12 months
Histrelin acetate (Vantas)	Prostate cancer - palliative therapy	1 implant (50 mg) SC for 12 months	1 implant/12 months

VI. Product Availability

Drug Name	Availability
Histrelin acetate (Supprelin LA)	Implant: 50 mg (approximately 65 mcg histrelin acetate per day over 12 months)
Histrelin acetate (Vantas)	Implant: 50 mg (approximately 50 mcg histrelin acetate per day over 12 months)

VII. References

1. Vantas Prescribing Information. Malvern, PA: Endo Pharmaceuticals Solutions, Inc.; December 2020. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/021732s023lbl.pdf. Accessed July 14, 2021.
2. Supprelin LA Prescribing Information. Malvern, PA: Endo Pharmaceuticals Solutions, Inc.; November 2019. Available at www.supprelinla.com. Accessed July 14, 2021.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at nccn.org. Accessed July 14, 2021.
4. National Comprehensive Cancer Network. Prostate Cancer Version 2.2020. Available at https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed July 14, 2021.
5. Kaplowitz P, Bloch C. Evaluation and referral of children with signs of early puberty. Pediatrics. 2016; 137(1): e20153732.
6. Carel JC, Eugster EA, Rogol A, et al. Consensus statement on the use of gonadotropin-releasing hormone analogs in children. Pediatrics. 2009;123(4):e752. Epub 2009 Mar 30.
7. 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. DOI: 10.1159/000501336.

8. Silverman LA, Neely EK, Kletter GB, et al. Long-term continuous suppression with once-yearly histrelin subcutaneous implants for the treatment of central precocious puberty: a final report of a phase 3 multicenter trial. J Clin Endocrinol Metab. 2015;100(6):2354-2363.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
4Q 2018 annual review: no significant changes; for prostate cancer, summarized NCCN and FDA-approved uses for improved clarity (limited to diagnosis) and added specialist involvement in care; references reviewed and updated.	08.07.18	11.18
4Q 2019 annual review: prostate cancer - modified language for failure of alternative GnRH agonist products to medical justification demonstrating inability to use these products, added urologist specialist option; per the formulary removed Zoladex and added Eligard as options for alternative drugs; references reviewed and updated.	08.01.19	11.19
4Q 2020 annual review: no significant changes; references reviewed and updated.	08.11.20	11.20
4Q 2021 annual review: no significant changes; for prostate cancer revised “Medical justification” to “Member must use” language; references reviewed and updated.	07.14.21	11.21

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.