Clinical Policy: Histrelin Acetate (Vantas, Supprelin LA)

Reference Number: PA.CP.PHAR.172
Effective Date: 01/18
Last Review Date: 10/18 Revision Log

Description
The intent of the criteria is to ensure that patients follow selection elements established by Pennsylvania Health and Wellness® medical policy for the use of histrelin acetate (Vantas® and Supprelin LA®).

FDA Approved Indication(s)
- Vantas is indicated for the palliative treatment of advanced prostate cancer.
- Supprelin LA is indicated for the treatment of children with central precocious puberty (CPP).

Policy/Criteria
It is the policy of Pennsylvania Health and Wellness that Vantas and Supprelin LA 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 Documentation showing a history of ≥ 3 months of gonadotropin-releasing hormone (GnRH) agonist injections that were effective and well tolerated (*See Appendix B*);
5 Request meets one of the following:
   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*).

Approval duration: 12 months
(One 12-month implant)

B. Central Precocious Puberty (must meet all):
1. Diagnosis of central precocious puberty 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/I (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. Member meets the following age requirements:
   a. Female: 2 - 11 years;
   b. Male: 2 - 12 years;
4. Prescribed by or in consultation with a pediatric endocrinologist;
5. Dose does not exceed 50 mg per 12 months (one implant per year).

Approval duration: 12 months
(One 12-month implant)

C. Gender Dysphoria (off-label) (must meet all):
1. Diagnosis of gender dysphoia as evidenced by meeting the DSM V criteria for gender dysphoria;
2. Prescribed by or in consultation with pediatric endocrinologist, adolescent medicine specialist or medication provider with experience and/or training in transgender medicine;
3. Member has psychological and social support during treatment;
4. Member does not suffer from a psychiatric comorbidity that interferes with the diagnostic work-up or treatment;
5. Member demonstrates consent and understanding of the exoected outcomes of GnRH analog treatment (*For minorities, when parental consent cannot be obtained, exceptions are reviewed on a case by case basis and in conjunction with a behavioral health provider*);
6. For adults: failure to achieve physiologic hormone levels or an intolerance with use of gender-affirming hormonal therapy (e.g., estrogen, testosterone).

Approval duration: 12 months

D. Other diagnoses/indications: Refer to CP.PMN.53 – off-label policy

II. Continued Approval

A. **Prostate Cancer** (must meet all):
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy applies (*see PA.LTSS.PHAR.01*);
2. Request is for Vantas;
3. Member is responding positively to therapy;
4. Request meets one of the following:
   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*).

Approval duration: 12 months
(One 12-month implant)

B. Central Precocious Puberty (must meet all):

1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy applies (*see PA.LTSS.PHAR.01*);
2. Request is for Supprelin LA;
3. Member is responding positively to therapy (e.g., decreased growth velocity, cessation of menses, softening of breast tissue or testes, arrested pubertal progression);
4. Member meets the following age requirement:
    a. Female: ≤ 11 years;
    b. Male: ≤ 12 years;
5. 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
(One 12-month implant)

C. Gender Dysphoria (off-label) (must meet all):
1. Currently receiving medication via Pennsylvania Health and Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy applies (*see PA.LTSS.PHAR.01*);
2. Member is responding positively to therapy;
3. Member has none of the following contraindications:
    a. Known hypersensitivity to GnRH, GnRH analogs, or any excipient in the requested product;
    b. Undiagnosed vaginal bleeding;
    c. Pregnancy or breast-feeding.

Approval duration: 12 months

D. Other diagnoses/indications (must meet 1 or 2):
1. Currently receiving medication via Pennsylvania Health and Wellness benefit and documentation supports positive response to therapy, or the Continuity of Care policy applies (*see PA.LTSS.PHAR.01*); or
2. Refer to CP.PMN.53 – off-label policy.

Background
Description/Mechanism of Action:
Histrelin acetate is a GnRH agonist that acts as a potent inhibitor of gonadotropin secretion when given continuously in therapeutic doses.

Formulations:
Histrelin acetate for subcutaneous administration:
Supprelin LA: 50 mg implant
- Designed to deliver approximately 65 mcg histrelin acetate per day over 12 months.

Vantas: 50 mg implant

- Designed to deliver approximately 50 mcg histrelin acetate per day over 12 months.

Appendices

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 for all relevant lines of business 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
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
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
Zoladex 3.6 (goserelin acetate)	Prostate Cancer - Palliative Therapy SC: 3.6 mg per 28 days	See regimen
Zoladex3.6, 10.8 (goserelin acetate)	Prostate Cancer - Stage B2-C SC: 3.6 mg, 8 weeks before radiotherapy, followed by 10.8 mg in 28 days (alternative: 4 injections of 3.6 mg at 28-day intervals, 2 preceding and 2 during radiotherapy)	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):
  - Vantas
    - Hypersensitivity to GnRH, GnRH agonist analogs, or any of the components in Vantas.
    - Use in women and pediatric patients.

    - Pregnancy
  - Suprelin LA
    - Hypersensitivity to gonadotropin releasing hormone (GnRH) or GnRH analogs.
    - Pregnancy
- Boxed warning(s): None reported

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9225	Histrelin implant (Vantas), 50 mg
J9226	Histrelin implant (Supprelin LA) 50mg

Reviews, Revisions, and Approvals	Date	Approval Date
4Q 2018 annual review: no significant changes; for oncology, summarized NCCN and FDA-approved uses for improved clarity (limited to diagnosis); specialist involvement in care and continuation of care added; references reviewed and updated.	08/18	

References
1. Vantas Prescribing Information. Malvern, PA: Endo Pharmaceuticals Solutions, Inc.; June 2017. Available at www.endo.com. Accessed July 30, 2018.
2. Supprelin LA Prescribing Information. Malvern, PA: Endo Pharmaceuticals Solutions, Inc.; May 2017. Available at www.supprelinla.com. Accessed July 30, 2018.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Histrelin acetate. Available at nccn.org. Accessed July 30, 2018.
4. National Comprehensive Cancer Network. Prostate cancer (Version 3.2018). Available at nccn.org. Accessed July 26, 2017.
5. Kaplowitz P, Bloch C. Evaluation and referral of children with signs of early puberty. Pediatrics. 2016; 137(1): e20153732.