Clinical Policy Title:	histrelin acetate
Policy Number:	RxA.296
Drug(s) Applied:	Vantas®, Supprelin® LA
Original Policy Date:	02/07/2020
Last Review Date:	04/18/2022
Line of Business Policy Applies to:	All lines of business

Background

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

- 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).

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
histrelin acetate (Supprelin® LA)	Central Precocious Puberty	1 implant (50 mg) inserted subcutaneously for 12 months	1 implant per 12 months
histrelin acetate (Vantas®)	Advanced prostate cancer palliative therapy	1 implant (50 mg) inserted subcutaneously for 12 months	1 implant per 12 months

Dosage Forms

- 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).

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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. 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
Commercial: 12 months
Medicaid: 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;
   b. Difference between bone age and chronological age was > 1 year (bone age versus 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: 2-11 years;
   b. Male: 2-12 years;
5. Dose does not exceed 50 mg per 12 months (one implant per year).

Approval Duration
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

A. Prostate Cancer (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Request is for Vantas®;
3. Member is responding positively to therapy;
4. If request is for a dose increase, 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 relevant off-label use (prescriber must submit supporting evidence).

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

Approval Duration
Commercial: 12 months
Medicaid: 12 months

B. Central Precocious Puberty (must meet all):

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Request is for Supprelin® LA;
3. 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;
4. Member meets one of the following age requirements (a or b):
   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

Commercial: 12 months

Medicaid: 12 months

III. 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

Below are suggested therapeutic alternatives based on clinical guidance. Please check drug formulary for preferred agents and utilization management requirements.

Drug Name	Dosing Regimen	Dose Limit/Maximum Dose
leuprolide acetate	Prostate Cancer - Palliative Therapy subcutaneously: 1 mg per day	1 mg per day
leuprolide acetate (Lupron Depot®)	Prostate Cancer - Palliative Therapy intramuscularly: 7.5 mg per 4 weeks, 22.5 mg per 12 weeks, 30 mg per 16 weeks, or 45 mg per 24 weeks	See dosing regimen
leuprolide acetate (Eligard®)	Prostate Cancer - Palliative Therapy subcutaneously: 7.5 mg per month, 22.5 mg per 3 months, 30 mg per 4 months, or 45 mg per 6 months	See dosing regimen
Zoladex®	Prostate cancer – Palliative Therapy 3.6 mg subcutaneously every 28 days 10.8 mg subcutaneously every 12 weeks	See dosing regimen
Trelstar®	Prostate cancer – 3.75 mg intramuscularly once every 4 weeks 11.25 mg intramuscularly once every 12 weeks 22.5 mg intramuscularly once every 24 weeks	See dosing regimen

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

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Hypersensitivity to GnRH, GnRH agonist analogs;
  - Supprelin® LA treatment increases the risk for pregnancy loss.

* Contraindications listed reflect direct statements made in the manufacturer's package insert; for additional uses, warnings, and precautions, please refer to clinical guidelines.

- Boxed Warning(s):
  - None reported.

APPENDIX D: General Information

- **Vantas®:**
  - Transient Increase in Serum Testosterone: Detected during the first week of treatment and may result in worsening of tumor symptoms.
  - Spinal Cord Compression and Urinary Tract Obstruction: May cause paralysis or renal impairment. Monitor patients at risk closely during therapy.
  - Difficulty Locating or Removing Implant: Loss of or inability to locate or remove an inserted implant has been reported. Caution is recommended.
  - Hyperglycemia and Diabetes: Hyperglycemia and an increased risk of developing diabetes have been reported in men receiving GnRH analogs. Monitor blood glucose level and manage according to current clinical practice.
  - Cardiovascular Diseases: Increased risk of myocardial infarction, sudden cardiac death and stroke has been reported in men. Monitor for cardiovascular disease and manage according to current clinical practice.
  - Effect on QT/QTc Interval: Androgen deprivation therapy may prolong the QT interval. Consider risks and benefits.
  - Embryo-Fetal Toxicity: Can cause fetal harm.
- **Supprelin® LA:**
  - Initial Agonistic Action: Initial transient increases of estradiol and/or testosterone may cause a temporary worsening of symptoms.
  - Psychiatric Events: Have been reported in patients taking GnRH agonists. Events include emotional lability, such as crying, irritability, impatience, anger, and aggression. Monitor for development or worsening of psychiatric symptoms.
  - Convulsions have been observed in patients receiving GnRH agonists with or without a history of seizures, epilepsy, cerebrovascular disorders, central nervous system anomalies or tumors, and in patients on concomitant medications that have been associated with convulsions.

References

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6. Goserelin acetate; In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2021. Accessed with subscription at: http://uptodate.com. Accessed January 11, 2022.
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Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1) Policy description table was updated. 2) Continued therapy criteria II.A.1 and II.B.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance…". 3) Initial therapy and continued therapy criteria were updated to include commercial and Medicaid separately. 4) Appendix B, therapeutic alternatives table was added. Alternative drugs were listed per NCCN prostate cancer guidelines. 5) Appendix C, contraindications was updated. 6) References updated.	06/25/2020	09/14/2020
Policy was reviewed: 1. Policy title table updated. 2. Clinical policy section standard verbiage was updated to include "The provision of prescriber samples…". 3. Continued therapy approval criteria II.A.1 was rephrased to "Member is currently receiving medication…". 4. Appendix B for therapeutic alternatives standard verbiage was updated to "Below are suggested therapeutic alternatives based on clinical guidance...". 5. Appendix D for general information was added. 6. References were updated.	05/11/2021	06/10/2021
Policy was reviewed: 1. Statement about provider sample ''The provision of provider samples does not guarantee coverage…" was added to Clinical Policy.	01/12/2022	04/18/2022

2. Appendix B, Updated: a. Drug Name: Updated to remove unavailable generic therapeutic alternative goserelin acetate, and triptorelin pamote. b. Dosing Regimen, Zoladex®: Updated dosing information from 10.8 mg subcutaneously every 12 weeks to 3.6 mg subcutaneously every 28 days, 10.8 mg subcutaneously every 12 weeks for indication Prostate cancer – Palliative Therapy. c. Appendix B, Maximum Dose, Zoladex®: Updated maximum dose information from 10.8 mg every 12 weeks to See dosing regimen for indication Prostate cancer – Palliative Therapy. d. Statement about drug listing format in Appendix B is rephrased to "Therapeutic alternatives are listed as generic (Brand name®) when the drug is available by both generic and brand; Brand name® when the drug is available by brand only and generic name when the drug is available by generic only". 3. Appendix C, Contraindications: Updated to remove contraindication Vantas® can cause fetal harm when used during pregnancy. 4. Disclaimer about contraindications "Contraindications listed reflect statements made in the manufacturer's package insert..." was added to Appendix C. 5. References were reviewed and updated.		