POLICY:

Gonadotropin-Releasing Hormone Agonists Implants

- Supprelin® LA (histrelin acetate subcutaneous implant – Endo Pharmaceuticals)
- Vantas® (histrelin acetate subcutaneous implant – Endo Pharmaceuticals Inc.)
- Zoladex® (goserelin acetate subcutaneous implant – AstraZeneca Pharmaceuticals)

APPROVAL DATE: 01/03/2019; Selected revision, 09/18/2019

OVERVIEW

Supprelin LA, Vantas, and Zoladex are gonadotropin-releasing hormone (GnRH) agonists implants. Vantas and Zoladex are indicated for the palliative treatment of advanced prostate cancer.1,2 Zoladex is also FDA-approved for use in combination with flutamide for the management of locally confined prostate cancer (3.6 mg and 10.8 mg implants). In addition, Zoladex 3.6 mg is indicated for the management of endometriosis, for use as an endometrial-thinning agent prior to endometrial ablation for dysfunction uterine bleeding, and for the palliative treatment of advanced breast cancer in pre- and perimenopausal women. Supprelin LA is a GnRH agonist indicated for the treatment of children with central precocious puberty.

Guidelines

The National Comprehensive Cancer Network (NCCN) prostate cancer guidelines (version 4.2018) list both Vantas and Zoladex as androgen deprivation therapy (ADT) therapy options for use in various settings (all category 2A), such as for adjuvant therapy, for treatment of regional disease, for patients who are on observation, in combination with antiandrogens (e.g., flutamide, bicalutamide) for neoadjuvant/adjuvant therapy as part of radiation treatment for localized disease, and as ADT for castration-naïve disease.2,3

The NCCN compendium and guidelines for breast cancer (version 3.2018) recommends use of gonadotropin-releasing hormone agonist such as Zoladex 3.6 mg implant in premenopausal women with hormone receptor-positive disease.

Central precocious puberty, also known as gonadotropin-dependent precocious puberty, is caused by early maturation of the hypothalamic-pituitary-gonadal axis.7 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 to review the use of GnRH agonists in pediatric patients with central precocious puberty (2009).8 The panel noted that the available GnRH agonists (including leuprolide and triptorelin) are effective despite different routes of administration, dosing, and duration of action. In addition, the various GnRH agonists are well-tolerated in children and adolescents.

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). Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below.

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, initial approval requires these agents to be prescribed by or in consultation with a physician who specializes in the condition being treated.
RECOMMENDED AUTHORIZATION CRITERIA
I. Coverage of Vantas is recommended in patients who meet the following criteria:

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

   **Dosing.** Approve one implant (50 mg) inserted subcutaneously in the upper arm.

   Vantas should be removed after 12 months of therapy; another implant can be inserted at that time to continue therapy.

   **Duration of Therapy:** Extended approvals are allowed if the patient continues to meet the criteria and dosing (see above). Another implant can be re-inserted if continuous therapy is needed.

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

FDA-Approved Indications
I. **Central Precocious Puberty.** Approve for 1 year.

   **Dosing.** Approve one implant (50 mg) inserted subcutaneously in the upper arm.

   Supprelin LA should be removed after 12 months of therapy; another implant can be inserted at that time to continue therapy.

   **Duration of Therapy:** Extended approvals are allowed if the patient continues to meet the criteria and dosing (see above). Another implant can be re-inserted if continuous therapy is needed.

   Discontinuation of Supprelin LA should be considered at the discretion of the physician and at the appropriate time point for the onset of puberty (approximately 11 years for females and 12 years for males).3
III. Coverage of Zoladex is recommended in patients who meet one of the following criteria:

FDA-Approved Indications

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

   **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 is implanted once every 28 days.
   
   B) Zoladex 10.8 mg is implanted once every 12 weeks.

   **Duration of Therapy:** Extended approvals are allowed if the patient continues to meet the criteria and dosing (see above).

2. **Breast Cancer.** Approve for 1 year if the patient meets the following conditions (A and B):

   A) Zoladex is used in premenopausal or perimenopausal women; AND
   
   B) The medication is prescribed by or in consultation with an oncologist.

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

   **Duration of Therapy:** Extended approvals are allowed if the patient continues to meet the criteria and dosing (see above).

3. **Endometriosis.** Approve for 6 months if the patient meets the following conditions (A and B):

   A) The patient is ≥ 18 years of age; AND
   
   B) The medication is prescribed by or in consultation with an obstetrician-gynecologist or a health care practitioner who specializes in the treatment of women’s health.

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

   **Duration of Therapy:** Up to a maximum of 6 months.

4. **Abnormal Uterine Bleeding.** Approve for 2 months if the patient meets the following conditions (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 health care practitioner who specializes in the treatment of women’s health.

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

   **Duration of Therapy:** Up to two depot implants given 4 weeks apart.

   When used as an endometrial-thinning agent prior to endometrial ablation, one or two depot implants are used. If only one implant is administered, surgery should be performed at 4 weeks. When two depot implants are administered (4 weeks apart), surgery should be performed within 2 to 4 weeks following the second depot implant.
**CONDITIONS NOT RECOMMENDED FOR APPROVAL**

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**


**HISTORY**

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<tr>
<th>Type of Revision</th>
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<td>New policy</td>
<td>-</td>
<td>01/03/2019</td>
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<tr>
<td>Selected revision</td>
<td>Revised Precocious Puberty (also known as GnRH-independent precocious puberty or peripheral precocious puberty) to Peripheral Precocious Puberty (also known as GnRH-independent precocious puberty).</td>
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