## Cigna Drug and Biologic Coverage Policy

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### Related Coverage Resources

- Somatropin (Genotropin®, Humatrope®, Norditropin FlexPro®, Nutropin®, Nutropin® AQ, Omnitrope®, Saizen®, Serostim®, Zomacton™, Zorbtive®)

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**INSTRUCTIONS FOR USE**

The following Coverage Policy applies to health benefit plans administered by Cigna companies. Coverage Policies are intended to provide guidance in interpreting certain standard Cigna benefit plans. Please note, the terms of a customer’s particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer’s benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer’s benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations. Proprietary information of Cigna. Copyright ©2017 Cigna

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**Coverage Policy**

Cigna covers histrelin acetate (Supprelin® LA) subcutaneous implant as medically necessary for the treatment of children with central precocious puberty (CPP) with onset of secondary sexual characteristics earlier than 8 years in females and 9 years in males. A stimulation test to confirm a diagnosis of CPP is required prior to initiation of treatment.

Cigna covers histrelin acetate (Supprelin® LA) subcutaneous implant as medically necessary for suppression of puberty in adolescents with gender dysphoria when ALL of the following criteria are met:

- Documented diagnosis of gender dysphoria or gender identity disorder fulfilling the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-V) criteria or International Classification of Diseases 10 (ICD-10) criteria
- Reached at least Tanner stage 2 of puberty
- Gender dysphoria has emerged or worsened with the onset of puberty.
- Absence of psychiatric comorbidity that would interfere with diagnosis or treatment
- Individual will have psychological and social support during treatment.
- Demonstrated knowledge and understanding of the expected outcomes of histrelin acetate (Supprelin® LA) treatment

Cigna does NOT cover histrelin acetate (Supprelin® LA) in combination with recombinant growth hormone (GH) to prolong the pre-pubertal state because this is considered not medically necessary.
When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to histrelin acetate subcutaneous implant (Supprelin® LA).

Note: Receipt of sample product does not satisfy any criteria requirements for coverage

**FDA Approved Indications**
Supprelin LA (histrelin acetate) subcutaneous implant is indicated for the treatment of children with central precocious puberty (CPP). Children with CPP (neurogenic or idiopathic) have an early onset of secondary sexual characteristics (earlier than 8 years of age in females and 9 years of age in males). They also show a significantly advanced bone age that can result in diminished adult height attainment.

Prior to initiation of treatment a clinical diagnosis of CPP should be confirmed by measurement of blood concentrations of total sex steroids, luteinizing hormone (LH) and follicle stimulating hormone (FSH) following stimulation with a GnRH analog, and assessment of bone age versus chronological age. Baseline evaluations should include height and weight measurements, diagnostic imaging of the brain (to rule out intracranial tumor), pelvic/testicular/adrenal ultrasound (to rule out steroid secreting tumors), human chorionic gonadotropin levels (to rule out a chorionic gonadotropin secreting tumor), and adrenal steroids to exclude congenital adrenal hyperplasia.

**FDA Recommended Dosing**
The recommended dose of Supprelin LA is one implant every 12 months. Each implant contains 50 mg histrelin acetate. The implant is inserted subcutaneously in the inner aspect of the upper arm and provides continuous release of histrelin (65 mcg/day) for 12 months of hormonal therapy. Supprelin LA should be removed after 12 months of therapy (the implant has been designed to allow for a few additional weeks of histrelin acetate release, in order to allow flexibility of medical appointments). At the time an implant is removed, another implant may be inserted to continue therapy. 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).

**Drug Availability**
Supprelin LA is available as a 50 mg histrelin acetate subcutaneous implant which delivers approximately 65 mcg histrelin acetate per day over 12 months.

**General Background**

**Pharmacology**
Like GnRH, Supprelin LA initially stimulates the pituitary gland to release luteinizing hormone (LH) and follicle stimulating hormone (FSH). Continuous exposure to Supprelin LA desensitizes the pituitary gland, decreasing LH and FSH release and gonadal steroid synthesis. Histrelin levels remain detectable and suppress gonadal steroid production for 12 months after implantation.

Histrelin is also available in the form of Vantas (a subcutaneous implant) and is approved for use in advanced prostate cancer. Currently Supprelin LA is not approved for use in advanced prostate cancer and Vantas is not approved for use in CPP. Supprelin LA releases at a rate of 65 mcg/day (the dosage required to be effective for CPP) while Vantas releases at a rate of 50-60 mcg daily (the dosage required to be effective for advanced prostate cancer).

**Guidelines**
- **The European Society for Pediatric Endocrinology and the Lawson Wilkins Pediatric Endocrine Society**
The European Society for Pediatric Endocrinology and the Lawson Wilkins Pediatric Endocrine Society issued a consensus statement for GnRH analogs including the 50 mg histrelin acetate implant. The conclusions of the consensus statement are a category CIII, a level of evidence that underscores the need for additional research in key areas such as the psychosocial effects of GnRH analog treatment for CPP. It was noted in the statement...
that the efficacy in increasing adult height is undisputed only in early-onset progressive CPP, which highlights the need to increase knowledge of the pathophysiology and normal limits of puberty and of the physical and psychosocial consequences of treated and untreated CPP and that the use of GnRH analogs for conditions other than CPP requires additional investigation and cannot be routinely suggested. (Carel, 2009)

- **Endocrine Society**
  The Endocrine Society published guidelines in 2009 regarding the treatment of transsexual persons that address the use of GnRH analogs for the treatment of adolescents. The guidelines recommend that adolescents who meet eligibility and readiness criteria for gender reassignment undergo treatment to suppress pubertal development and that treatment begin when girls and boys first demonstrate physical changes of puberty (confirmed by pubertal levels of estradiol and testosterone, respectively and no earlier than Tanner stages 2-3) and when pubertal changes have resulted in an increase of their gender dysphoria. The recommended treatment to suppress pubertal hormones is GnRH analogs. (Hembree 2009)

  The Endocrine Society state that adolescents are eligible and ready for GnRH treatment when meeting the following criteria:
  1. Fulfill DSM IV-TR or ICD-10 criteria for GID or transsexualism.
  2. Have experienced puberty to at least Tanner stage 2.
  3. Have (early) pubertal changes that have resulted in an increase of their gender dysphoria.
  4. Do not suffer from psychiatric comorbidity that interferes with the diagnostic work-up or treatment.
  5. Have adequate psychological and social support during treatment, AND
  6. Demonstrate knowledge and understanding of the expected outcomes of GnRH analog treatment, cross-sex hormone treatment, and sex reassignment surgery, as well as the medical and the social risks and benefits of sex reassignment.

  Adolescents are eligible for cross-sex hormone treatment if they:
  1. Fulfill the criteria for GnRH treatment, AND
  2. Are 16 years or older.

  Readiness criteria for adolescents eligible for cross-sex hormone treatment are the same as those for adults. (Hembree, 2009)

- **World Professional Association for Transgender Health (WPATH)**
  The WPATH provides criteria for puberty-suppressing hormones for adolescents. The criteria include the following elements:
  1. The adolescent has demonstrated a long-lasting and intense pattern of gender nonconformity or gender dysphoria (whether suppressed or expressed);
  2. Gender dysphoria emerged or worsened with the onset of puberty;
  3. Any coexisting psychological, medical, or social problems that could interfere with treatment (e.g., that may compromise treatment adherence) have been addressed, such that the adolescent's situation and functioning are stable enough to start treatment;
  4. The adolescent has given informed consent and, particularly when the adolescent has not reached the age of medical consent, the parents or other caretakers or guardians have consented to the treatment and are involved in supporting the adolescent throughout the treatment process.

  (WPATH, 2012)

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**Coding/Billing Information**

**Note:**
1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

**Covered when medically necessary:**

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<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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<tr>
<td>J9226</td>
<td>Histrelin implant (Supprelin LA), 50 mg</td>
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References


