



CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

Subject Histrelin acetate subcutaneous implant (Supprelin LA)

Effective Date3/15/2011
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Coverage Position Number..... 8008

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INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement (GSA), 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 supercedes** 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. Proprietary information of CIGNA. Copyright ©2011 CIGNA

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.

When covered and medically necessary, the dosage, frequency of insertion, and duration of therapy 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) therapy.

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.

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 supplied in a corrugated shipping carton that contains 2 inner cartons: a small one for the vial containing the Supprelin LA implant, which is shipped with a cold pack inside a polystyrene cooler that must be refrigerated upon arrival, and a larger one comprising the Implantation Kit, which must *not* be refrigerated, for use during insertion or removal of Supprelin LA. The Supprelin LA implant carton contains an opaque amber plastic pouch. Inside the pouch is a 3.5 mL clear glass vial with a Teflon-coated stopper and an aluminum seal, containing the hydrated implant immersed in 2 mL of sterile 1.8% sodium chloride solution.

General Background

Disease Overview

Supprelin LA is a gonadotropin releasing hormone (GnRH) analog approved for treatment of CPP in children. Children with CPP enter puberty earlier than children without CPP. Children with CPP also exhibit increased bone age and height velocity, yet ultimately attain a decreased adult height compared to normal adults.

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 primarily metabolized via hepatic C-terminal dealkylation and hydrolysis.

Guidelines

Histrelin is 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).

Clinical Efficacy

Supprelin LA has been evaluated in two case series, including a total of 47 patients, some previously treated and some treatment-naïve. In treatment-naïve patients, Supprelin LA significantly decreased stimulated LH (27.6 mIU/mL), stimulated FSH (13.4 mIU/mL), estradiol (18.7 pg/mL), and bone age relative to chronological age (0.08 years) from baseline. In treatment-experienced patients, Supprelin LA significantly decreased basal LH (0.27 mIU/mL), stimulated LH (1.02 – 1.6 mIU/mL), stimulated FSH (0.55 – 1.3 mIU/mL), estradiol (3.31 pg/mL), breast development (Tanner stage 0.6), and bone age relative to chronological age (0.09 years) from baseline. No trials directly compare Supprelin LA to other available CPP treatments.

Adverse Reactions

No drug interaction data are available for Supprelin LA, Vantas, or other GnRH analogs leuprolide and goserelin. A potential interaction exists between triptorelin and drugs that cause hyperprolactinemia (ie, risperidone, prochlorperazine, olanzapine, haloperidol, chlorpromazine, metoclopramide, methyl dopa). Concomitant use of these agents may result in decreased efficacy of triptorelin or other GnRH agonists because hyperprolactinemia reduces the number of GnRH receptors.

Implant site reactions are the most commonly reported adverse events in clinical trials with Supprelin LA. These reactions include pain, soreness, bruising, erythema, and swelling. Other commonly reported adverse reactions include scar, keloid scar, suture complications, post-procedural pain, and site pain. Serious adverse events include benign pituitary tumor, amblyopia, and implantation-site infection. Metrorrhagia was reported as possibly related to treatment in two patients. The efficacy of Supprelin LA may be reduced with concomitant administration of drugs that cause hyperprolactinemia (ie, antipsychotics, methyl dopa, metoclopramide).

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Covered when medically necessary:

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

ICD-9-CM Diagnosis Codes	Description
259.1	Precocious sexual development and puberty, not elsewhere classified

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Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare Great-West Healthcare	8/15/2008	8008	Histrelin acetate subcutaneous implant (Supprelin LA)

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