Neighborhood Health Plan OF RHODE ISLAND™
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Supprelin® LA (histrelin)
(Subcutaneous Implant)

Date of Origin: 06/01/2025
Dates Reviewed: 04/2025
Medical Scope: Medicaid, Commercial, MMP

I. Length of Authorization

Coverage will be provided for 12 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Supprelin LA 50 mg implant: 1 implant per 12 months

B. Max Units (per dose and over time) [HCPCS Unit]:

- 1 billable unit (50 mg) per 12 months

III. Summary of Evidence

Supprelin LA is a gonadotropin releasing hormone (GnRH) agonist indicated for the treatment of children with central precocious puberty (CPP). Two single-arm, open label studies evaluated efficacy. Study 1 was conducted in 11 pretreated female patients, 3.7 to 11.0 years of age, while Study 2 was conducted in 36 patients (33 females and 3 males), 4.5 to 11.6 years of age, with 20 being treatment-naïve. Efficacy assessments were similar in both studies and included endpoints that measured the suppression of gonadotropins (luteinizing hormone and follicle stimulating hormone) and gonadal sex steroids (estrogen in girls and testosterone in boys, respectively) on treatment. Other assessments were clinical (evidence of stabilization or regression of signs of puberty) or gonadal steroid-dependent (bone age, linear growth). In Study 2, suppression of LH was induced in all treatment naïve subjects and maintained in all pretreated subjects at Month 1 after implantation and continued through Month 12 (suppression was defined as a peak LH < 4 mIU/mL following stimulation with the GnRH analog leuprolide acetate). The most common adverse reaction is implant site reaction (51.1%), including complications related to the insertion or removal of the implant.

IV. Initial Approval Criteria

Coverage is provided in the following conditions:

Universal Criteria [1]

- MMP members who have previously received this medication within the past 365 days are not subject to Step Therapy Requirements; **AND**
- Patient does not have a hypersensitivity to gonadotropin releasing hormone (GnRH) or GnRH analog type medications; **AND**

Central Precocious Puberty (CPP) † Φ [1-6]

- Patient is between the ages of 2 and less than 13 years; **AND**
- Will not be used in combination with growth hormone; **AND**
- Onset of secondary sexual characteristics earlier than age 8 for females and 9 for males associated with pubertal pituitary gonadotropin activation; **AND**
- Diagnosis is confirmed by pubertal gonadal sex steroid levels and a pubertal luteinizing hormone (LH) response to stimulation by native GnRH; **AND**
- Bone age advanced greater than 2 standard deviations (SD) beyond chronological age; **AND**
- Tumor has been ruled out by lab tests such as diagnostic imaging of the brain (to rule out intracranial tumor), pelvic/testicular/adrenal ultrasound (to rule out steroid secreting tumors), and human chorionic gonadotropin levels (to rule out a chorionic gonadotropin secreting tumor)
- The patient has experienced an inadequate treatment response, intolerance, or is contraindicated to treatment with Lupron Depot-Ped (leuprolide)

Gender Dysphoria (formerly Gender Identity Disorder) ‡ [7,9,10]

- Patient has experienced puberty development to at least Tanner stage 2 (*Note: this applies only to patients <18 years of age);* **AND**
- Patient has a diagnosis of gender dysphoria as confirmed by a qualified mental health professional (MHP)****** OR the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) Criteria §; **AND**
- A qualified MHP****** has confirmed all of the following:
    - Patient has demonstrated a long-lasting and intense pattern of gender nonconformity or gender dysphoria (whether suppressed or expressed); **AND**
    - Gender dysphoria worsened with the onset of puberty; **AND**
    - 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; **AND**
    - Patient has sufficient mental capacity to give informed consent to this (reversible) treatment; **AND**
- Patient has been informed of the effects and side effects of treatment (including potential loss of fertility if the individual subsequently continues with sex hormone treatment) and options to preserve fertility; **AND**

- Patient has given informed consent and (particularly when the adolescent has not reached the age of legal medical consent, depending on applicable legislation) the parents or other caretakers or guardians have consented to the treatment and are involved in supporting the adolescent throughout the treatment process; **AND**
- A pediatric endocrinologist or other clinician experienced in pubertal assessment has confirmed all of the following:
    - Agreement in the indication for treatment; **AND**
    - There are no medical contraindications to treatment

**** Definition of a qualified mental health professional** [10]

- Are licensed by their statutory body and hold, at a minimum, a master's degree or equivalent training in a clinical field relevant to this role and granted by a nationally accredited statutory institution; **AND**
- For countries requiring a diagnosis for access to care, the health care professional should be competent using the latest edition of the World Health Organization's International Classification of Diseases (ICD) for diagnosis. In countries that have not implemented the latest ICD, other taxonomies may be used; efforts should be undertaken to utilize the latest ICD as soon as practicable; **AND**
- Are able to identify co-existing mental health or other psychosocial concerns and distinguish these from gender dysphoria, incongruence, and diversity; **AND**
- Are able to assess capacity to consent for treatment; **AND**
- Have experience or be qualified to assess clinical aspects of gender dysphoria, incongruence, and diversity; **AND**
- Undergo continuing education in health care relating to gender dysphoria, incongruence, and diversity

§ DSM-V Criteria for Gender Dysphoria [7,9]

- A marked incongruence between one's experienced/expressed gender and natal gender of at least 6mo in duration, as manifested by at least TWO of the following:
    - A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex characteristics (or in young adolescents, the anticipated secondary sex characteristics)
    - A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender (or in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics)
    - A strong desire for the primary and/or secondary sex characteristics of the other gender
    - A strong desire to be of the other gender (or some alternative gender different from one's designated gender)
    - A strong desire to be treated as the other gender (or some alternative gender different from one's designated gender)

- A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's designated gender); **AND**
- The condition is associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning; **AND**
- Specify one of the following:
  - The condition exists with a disorder of sex development; **OR**
  - The condition is post-transitional, in that the individual has transitioned to full-time living in the desired gender (with or without legalization of gender change) and has undergone (or is preparing to have) at least one sex-related medical procedure or treatment regimen—namely, regular sex hormone treatment or gender reassignment surgery confirming the desired gender (e.g., penectomy, vaginoplasty in natal males; mastectomy or phalloplasty in natal females).

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s); **Φ** Orphan Drug

V. Renewal Criteria [1]

Coverage can be renewed based on the following criteria:

- Patient continues to meet the universal criteria and other indication-specific relevant criteria identified in section IV; **AND**
- Absence of unacceptable toxicity from the drug. Example of unacceptable toxicity include: severe implant site reactions, convulsions/seizures, psychiatric events (e.g., emotional lability including crying, irritability, impatience, anger, and aggression), signs and symptoms of pseudotumor cerebri/idiopathic intracranial hypertension (e.g., headaches, papilledema, blurred vision, diplopia, vision loss, eye pain, tinnitus, dizziness, and nausea); etc.; **AND**

Central Precocious Puberty (CPP) [4-6]

- Patient is less than 13 years of age; **AND**
- Disease response as indicated by lack of progression or stabilization of secondary sexual characteristics, decrease in height velocity, a decrease in the ratio of bone age to chronological age (BA:CA), and improvement in final height prediction

Gender Dysphoria [7,9,10]

- Patient has shown a beneficial response to treatment as evidenced by routine monitoring of clinical pubertal development and applicable laboratory parameters

VI. Dosage/Administration [1]

Indication	Dose
CPP and Gender Dysphoria	1 implant (50 mg) inserted subcutaneously every 12 months

VII. Billing Code/Availability Information

HCPCS Code:

- J9226 – Histrelin implant (Supprelin LA), 50 mg; 1 billable unit = 50 mg

NDC:

- Supprelin LA 50 mg implant 67979-0002-xx

VIII. References

1. Supprelin LA [package insert]. Chadds Ford, PA; Endo Pharmaceuticals Solutions; April 2022. Accessed April 2025.
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4. Brito VN, Spinola-Castro AM, Kochi C, et al. Central precocious puberty: revisiting the diagnosis and therapeutic management. Arch Endocrinol Metab. 2016 Apr;60(2):163-72
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7. Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2017; 102:3869.
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9. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Arlington, VA: American Psychiatric Association Publishing.
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11. Harrington J, Palmert MR. (2024). Treatment of Precocious Puberty. In Snyder PJ, Geffner ME (Eds.), *UpToDate*. Last updated May 1, 2024. Accessed on June 10, 2024. Available from: https://www.uptodate.com/contents/treatment-of-precocious-puberty?search=Treatment%20of%20precocious%20puberty&source=search_result&selectedTitle=1~119&usage_type=default&display_rank=1

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
E30.1	Precocious puberty
E30.8	Other disorders of puberty
F64.0	Transsexualism
F64.1	Dual role transvestism
F64.2	Gender identity disorder of childhood
F64.8	Other gender identity disorders
F64.9	Gender identity disorder, unspecified

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

The preceding information is intended for non-Medicare coverage determinations. Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determinations (NCDs) and/or Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. Local Coverage Articles (LCAs) may also exist for claims payment purposes or to clarify benefit eligibility under Part B for drugs which may be self-administered. The following link may be used to search for NCD, LCD, or LCA documents: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications, including any preceding information, may be applied at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

Policy Rationale:

Supprelin LA was reviewed by the Neighborhood Health Plan of Rhode Island Pharmacy & Therapeutics (P&T) Committee. Neighborhood adopted the following clinical coverage criteria to ensure that its members use Supprelin LA according to Food and Drug Administration (FDA) approved labeling and/or relevant clinical literature. Neighborhood worked with network prescribers and pharmacists to draft these criteria. These criteria will help ensure its members are using this drug for a medically accepted indication, while minimizing the risk for adverse effects and ensuring more cost-effective options are used first, if applicable and appropriate. For INTEGRITY (Medicare-Medicaid Plan) members, these coverage criteria will only apply in the absence of National Coverage Determination (NCD) or Local Coverage Determination (LCD) criteria. Neighborhood will give individual consideration to each request it reviews based on the information submitted by the prescriber and other information available to the plan.