



State of California—Health and Human Services Agency
Department of Health Care Services



GAVIN NEWSOM
GOVERNOR

DATE: November 17, 2020

N.L.: 08-1120

Supersedes N.L.: 04-1019

Index: Benefits

TO: All County California Children's Services Program Administrators,
Medical Directors, and Integrated Systems of Care Division Staff

SUBJECT: California Children's Services Program coverage of treatment for Central
Precocious Puberty - Revised

I. PURPOSE

The purpose of this Numbered Letter (N.L.) is to define California Children's Services Program (CCS) coverage of Gonadotropin-Releasing Hormone (GnRH) Agonists prescribed for the treatment of Central Precocious Puberty (CPP).

The CCS Program publishes this N.L. under the program's authority to authorize services that are medically necessary to treat CCS-eligible conditions.^{1,2,3}

II. BACKGROUND

CPP⁴ is defined as the early maturation of the hypothalamic-pituitary-gonadal axis, leading to early onset of secondary sexual characteristics, before the age of 8 years in girls or 9 years in boys.

Causes include, but are not limited to, hypothalamic hamartoma, (optic) glioma and various other central nervous system tumors, suprasellar arachnoid cyst, hydrocephalus, neurofibromatosis type 1, tuberous sclerosis, septo-optic dysplasia (optic nerve hypoplasia), Chiari II malformations, myelomeningocele, granulomatous disease, cerebral palsy, and sequelae of other CCS-eligible conditions including central nervous system irradiation.

Evaluation of CPP is typically done when a female has breast development, accelerated height velocity, and crosses a growth chart percentile before age 8 years, or when a male has both testicular and penile enlargement before age 9 years. Additional diagnostic studies performed by CCS-paneled endocrinologists generally include basal (early-morning) levels of luteinizing hormone (LH), follicle-stimulating hormone (FSH), estradiol in girls, testosterone in boys, and, as appropriate, GnRH stimulation test with basal and stimulated LH/FSH and estradiol

in girls and testosterone in boys. Other studies may include measurement of adrenal steroids, pelvic and adrenal imaging, and rarely, contrast-enhanced head magnetic resonance imaging (MRI), or genetic testing.

Imaging studies may be ordered as part of the diagnostic process, including a contrast-enhanced brain MRI to rule out the presence of intracranial pathology (at the discretion of the pediatric endocrinologist) and/or a pelvic/adrenal ultrasound to rule out a steroid-secreting gonadal or adrenocortical tumor. Rarely, other imaging may be required to rule out a human chorionic gonadotropin-secreting tumor.

Treatment of CPP consists of a GnRH agonist which may be administered intramuscularly or by implant.⁵ See Attachment, “GnRH Agonist Treatment Options,” for specific drug information. The GnRH agonist provides continuous stimulation to the pituitary gonadotroph cells which leads to their desensitization, resulting in decreased production of LH and FSH and, in turn, decreased production of sex hormones (estradiol in girls and testosterone in boys).

III. POLICY

- A. CCS clients are eligible to receive GnRH agonist therapy when all of the following criteria are met:
1. The client is between the ages of 2 and 10 years at the time of initial evaluation.
 2. The client has been evaluated by a CCS-paneled endocrinologist at an endocrinology Special Care Center (SCC).
 3. The diagnosis of CPP is made by the CCS-paneled endocrinologist at the SCC based on age of pubertal onset, rate of progression of pubertal changes, height velocity, and bone age (advanced more than two standard deviations above chronological age) or bone age acceleration (advancing more than one year per chronological year).
 4. The diagnosis is confirmed when the client has one of the following laboratory findings:
 - a. Serum LH level exceeds prepubertal level (generally greater than 0.2 – 0.3 international units per litre (IU/L), depending on the assay used).
 - b. A positive GnRH stimulation test, defined by a peak LH level greater than or equal to 3.3 – 5 IU/L, depending on the assay, or a pubertal level of estradiol (girls) or testosterone (boys) detected (usually) 18 – 24 hours after the GnRH administration.

5. The GnRH agonist is prescribed by the CCS-paneled endocrinologist at an SCC.
- B. When the conditions described in section III.A. are met, GnRH agonist treatment is medically necessary and shall be authorized as follows:
1. Initial authorization shall be for a standard GnRH agonist consistent with Pediatric Endocrine Society recommendations which are listed in the Attachment, "GnRH Agonist Treatment Options."
 2. Re-authorization of GnRH agonist therapy shall be every 12 months or until the CCS program eligibility end-date, as long as it is deemed efficacious demonstrated by plateauing or reversal of relevant pubertal changes on physical examination, persistent biochemical suppression of the hypothalamic-pituitary-gonadal axis, and continued predicted increase in adult height.

C. Additional considerations for medical necessity determination:

For clients who do not meet the criteria described in sections III.A. or III.B., SCCs may demonstrate medical necessity by submitting any other clinical documentation and/or evidence that would support the initial or reauthorization of the client's GnRH agonist therapy. SCCs or pharmacies should submit this documentation to the Integrated Systems of Care Division (ISCD) Medical Director or designee.

D. Whole Child Model (WCM) Counties:

For CCS clients who are enrolled in a Medi-Cal managed care plan (MCP) and reside in a WCM county, the client's MCP shall be responsible for authorizing, coordinating, and covering GnRH agonist therapy. MCPs operating in WCM counties should use the authorization guidelines described in this N.L., or utilize the MCP's existing GnRH agonist therapy policies, whichever is less restrictive.

IV. POLICY IMPLEMENTATION

- A. For non-Whole Child Model (WCM) independent counties, requests for authorization of GnRH agonist treatment will be reviewed and authorized by county CCS Programs.
- B. For dependent counties, requests for authorization of GnRH agonist treatment will be reviewed and authorized by the ISCD Special Populations Unit at CCSExpeditedReview@dhcs.ca.gov; or to secure RightFax number RightFax (916) 440-5306.

- C. For WCM counties, requests for authorization of GnRH agonist treatment will be reviewed and authorized by the Managed Care Plan (MCP) and requests for authorization should be directed to the appropriate authorization county-specific MCP authorization unit.

Beginning April 1, 2021, all requests for prior authorization of medications billed by National Drug Code and dispensed by a Medi-Cal enrolled pharmacy provider, shall be sent from the pharmacy provider to the Medi-Cal Rx vendor, Magellan Medicaid Administration, Inc. (Magellan). The Medi-Cal RX website provides guidance: <https://medi-calrx.dhcs.ca.gov/home/>.

If you have any questions regarding this N.L., please contact the ISCD Medical Director or designee at ISCD-MedicalPolicy@dhcs.ca.gov.

Sincerely,

ORIGINAL SIGNED BY

Roy Schutzengel
Medical Director
Integrated Systems of Care Division

Attachment(s):
GnRH Agonist Treatment Options

¹ 22 Cal. Code Regs. § 41515.1 et. seq. Determination of Medical Eligibility
<https://govt.westlaw.com/calregs/Document/I28E30090D4B811DE8879F88E8B0DAAAE?viewType=FullText&originalContext=documenttoc&transitionType=CategoryPageItem&contextData=%28sc.Default%29>

² 22 Cal. Code Regs. § 41700 Availability
[https://govt.westlaw.com/calregs/Document/I2F1A7E70D4B811DE8879F88E8B0DAAAE?viewType=FullText&originalContext=documenttoc&transitionType=CategoryPageItem&contextData=\(sc.Default\)&bhcp=1&ignorebhwarn=IgnoreWarns](https://govt.westlaw.com/calregs/Document/I2F1A7E70D4B811DE8879F88E8B0DAAAE?viewType=FullText&originalContext=documenttoc&transitionType=CategoryPageItem&contextData=(sc.Default)&bhcp=1&ignorebhwarn=IgnoreWarns)

³ 22 Cal. Code Regs. § 41740 Eligibility for Treatment Services
<https://govt.westlaw.com/calregs/Document/I2FDD8050D4B811DE8879F88E8B0DAAAE?viewType=FullText&originalContext=documenttoc&transitionType=StatuteNavigator&contextData=%28sc.Default%29>

⁴ AAP Clinical Report, Evaluation and Referral of Children with Signs of Early Puberty, 2016
<https://pediatrics.aappublications.org/content/pediatrics/137/1/e20153732.full.pdf>

⁵ Treatment of Central Precocious Puberty
Erica A Eugster. *Journal of the Endocrine Society*, Volume 3, Issue 5, May 2019, Pages 965–972, Published: 28 March 2019.
<https://academic.oup.com/jes/article/3/5/965/5421014>

**GnRH Agonist Treatment Options
June 1, 2019**

Drug	Route of Administration	Frequency
Leuprolide acetate (Lupron Depot-Ped)	intramuscular	every 1-3 months
Histrelin acetate (Supprelin)	implant	every 12 months
Triptorelin pamoate (Triptodur)	intramuscular	every 6 months