

**Medical Necessity Letter**

The guidance presented here is for informational purposes only and is not intended to provide reimbursement or legal advice. AbbVie does not guarantee that the use of any information provided will result in coverage or payment by any third-party payer. You are responsible for the submission based on your clinical judgment.

**Indication for LUPRON DEPOT-PED® (leuprolide acetate for depot suspension)**

LUPRON DEPOT-PED 7.5 mg, 11.25 mg, and 15 mg for 1-month and 11.25 mg and 30 mg for
3-month administration are indicated in the treatment of children with central precocious puberty (CPP).

CPP is defined as early onset of secondary sexual characteristics (generally earlier than 8 years of age in girls and 9 years of age in boys) associated with pubertal pituitary gonadotropin activation. It may show a significantly advanced bone age that can result in diminished adult height.

Prior to initiation of treatment, confirm diagnosis of CPP by testing luteinizing hormone (LH) and sex steroid levels, and assess bone age versus chronological age. Baseline evaluations should be done to rule out intracranial tumor, steroid secreting tumors, a chorionic gonadotropin secreting tumor, and congenital adrenal hyperplasia.

**Important Safety Information for LUPRON DEPOT-PED**

LUPRON DEPOT-PED is contraindicated in:

* Patients with hypersensitivity to GnRH, GnRH agonist, or any of the excipients. Anaphylactic reactions to GnRH agonists have been reported in the medical literature.
* Females who are or may become pregnant during treatment, as it may cause fetal harm.

During the early phase of therapy, gonadotropins and sex steroids rise above baseline because of the initial stimulatory effect of the drug. An increase in clinical signs and symptoms of puberty may be observed.

Psychiatric events have been reported in patients taking GnRH agonists, including LUPRON DEPOT-PED. Events include emotional lability, such as crying, irritability, impatience, anger, and aggression. Monitor for development or worsening of psychiatric symptoms during treatment.

Postmarketing reports of convulsions have been observed in patients receiving GnRH agonists, including LUPRON DEPOT-PED. These included patients with a history of seizures, epilepsy, cerebrovascular disorders, central nervous system anomalies or tumors, and patients on concomitant medications that have been associated with convulsions, such as bupropion and SSRIs. Convulsions have also been reported in patients in the absence of any of the conditions mentioned above.

Monitor adequate response with a GnRHa stimulation test, basal LH, or serum concentration of sex steroid levels:

* After 1-2 months of initiating therapy for 1-month formulations
* After 2-3 months of initiating therapy and at month 6 for 3-month formulations
* For both formulations, ensure adequate suppression with each dose change or as judged clinically appropriate. Measure for height and bone advancement every 6-12 months

Noncompliance with drug regimen or inadequate dosing may result in inadequate control of the pubertal process with gonadotropins and/or sex steroids increasing above prepubertal levels.

The most common adverse reactions with GnRH agonists including LUPRON DEPOT-PED are injection site reactions/pain including abscess, general pain, headache, emotional lability, and hot flushes/sweating. The most frequent adverse reactions (≥2%) in LUPRON DEPOT-PED clinical studies were:

* LUPRON DEPOT-PED 7.5 mg, 11.25 mg and 15 mg for 1-month administration: injection site reactions including abscess, emotional lability, acne/seborrhea, vaginitis/vaginal bleeding/vaginal discharge, pain, rash including erythema multiforme, headache, and vasodilation.
* LUPRON DEPOT-PED 11.25 mg, and 30 mg for 3-month administration: injection site pain, increased weight, headache, altered mood, and injection site swelling.

Diagnostic tests of pituitary gonadotropic and gonadal functions conducted during treatment and up to 6 months after discontinuation may be affected.

LUPRON DEPOT-PED must be administered under the supervision of a physician.

The use of LUPRON DEPOT-PED in children under 2 years of age is not recommended.

**SAMPLE Letter of Medical Necessity**

<VARIABLE DATE>

<VARIABLE PAYER NAME>

<VARIABLE PAYER ADDRESS>

<VARIABLE CITY, STATE>

<VARIABLE PAYER FAX NUMBER>

Attn: <VARIABLE ATTN>

Re: Coverage of LUPRON DEPOT-PED (leuprolide acetate for depot suspension) <VARIABLE STRENGTH AND DURATION>

<VARIABLE PATIENT NAME>

<VARIABLE PATIENT DATE OF BIRTH>

<VARIABLE PATIENT MEMBER ID>

To whom it may concern,

I am writing to request approval of LUPRON DEPOT-PED <VARIABLE Strength> <Variable Duration> (leuprolide acetate for depot suspension) to treat my patient <VARIABLE PATIENT NAME> for Central Precocious Puberty (CPP). The full prescribing information for Lupron Depot-PED can be accessed at rxabbvie.com.

This product was denied on <VARIABLE DATE> for the following reason(s): <VARIABLE CONTENT>. <VARIABLE
PATIENT NAME> is a <VARIABLE PATIENT AGE> year-old who has been diagnosed with central precocious puberty.

<VARIABLE PATIENT NAME>’s medical history includes the following:

<DESCRIBE THE PATIENT’s MEDICAL HISTORY, DIAGNOSIS, ETC.

 **Prior Treatment History:** <CONTENT>

**Clinical Considerations** (choose only one)

**Clinical Consideration: Patient has a clinical diagnosis of CPP and is treatment naïve.**

LUPRON DEPOT-PED is indicated in the treatment of children with central precocious puberty (CPP).

Patient has not had hypersensitivity to GnRH, GnRH agonists or any of the excipients in LUPRON DEPOT-PED, and is not pregnant or planning to become pregnant.

**LUPRON DEPOT-PED 7.5 mg, 11.25 mg, or 15 mg for 1-month administration**

* During the treatment period, LUPRON DEPOT-PED suppressed gonadotropins and sex steroids to prepubertal levels. Suppression of peak stimulated LH concentrations to < 1.75 mIU/mL was achieved in 96% of subjects by month 1.
* In females, suppression of breast development ranged from 66.7 to 90.6% of subjects during the first 5 years of treatment. The mean stimulated estradiol was 15.1 pg/mL at baseline, decreased to the lower level of detection (5.0 pg/mL) by Week 4 and was maintained there during the first 5 years of treatment.
* In males, suppression of genitalia development ranged from 60% to 100% of subjects during the first 5 years of treatment. The mean stimulated testosterone was 347.7 ng/dL at baseline and was maintained at levels no greater than 25.3 ng/dL during the first 5 years of treatment.
* Through year 5, the mean growth rate ranged between 3.4 and 5.6 cm/yr. The mean ratio of bone age to chronological age decreased from 1.5 at baseline to 1.1 by end of treatment. The mean height standard deviation score changed from 1.6 at baseline to 0.7 at the end of the treatment phase

**LUPRON DEPOT-PED 11.25 mg or 30 mg for 3-month administration**

* The percentage of overall subjects with suppression of peak-stimulated LH to < 4.0 mIU/mL, as determined by assessments at months 2, 3 and 6 is 78.6% in the 11.25 mg dose and 95.2% in the 30 mg dose.
* The percentage of treatment naïve subjects with suppression of peak-stimulated LH to < 4.0 mIU/mL, as determined by assessments at months 2, 3 and 6 is 76.2 % in the 11.25 mg dose and 90.5% in the 30 mg dose.
* For the LUPRON DEPOT-PED 11.25 mg dose for 3-month administration, 93% (39/42) of subjects and for LUPRON DEPOT-PED 30 mg dose for 3-month administration 100% (42/42) of subjects had sex steroid (estradiol or testosterone) suppressed to prepubertal levels at all visits.
* Clinical suppression of puberty in female patients was observed in 29 of 32 (90.6%) and 28 of 34 (82.4%) of patients in the 11.25 mg and 30 mg groups, respectively, at month 6.
* Clinical suppression of puberty in males was observed in 1 of 2 (50.0%) and 2 of 5 (40.0%) patients in the 11.25 mg and 30 mg groups, respectively, at month 6.
* In subjects with complete data for bone age, 29 of 33 (87.9 %) in the 11.25 mg group and 30 of 40 in the 30 mg group (75.0% ) had a decrease in the ratio of bone age to chronological age at month 6 compared to screening.

For additional information on this topic, please contact AbbVie Medical Information ([www.abbviemedinfo.com](http://www.abbviemedinfo.com)).

**Clinical Consideration: Patient treatment intolerance or previous treatment failure**

LUPRON DEPOT-PED is indicated in the treatment of children with central precocious puberty (CPP).

Patient does not have hypersensitivity to GnRH, GnRH agonists or any of the excipients in LUPRON DEPOT-PED, and is not pregnant or planning to become pregnant.

**LUPRON DEPOT-PED 11.25 mg or 30 mg for 3-month administration**

* The percentage of overall subjects with suppression of peak-stimulated LH to < 4.0 mIU/mL, as determined by assessments at months 2, 3 and 6 is 78.6% in the 11.25 mg dose and 95.2% in the 30 mg dose.
* The percentage of treatment experienced subjects with suppression of peak-stimulated LH to < 4.0 mIU/mL, as determined by assessments at months 2, 3 and 6 is 81.0 % in the 11.25 mg dose and 100% in the 30 mg dose.
* For the LUPRON DEPOT-PED 11.25 mg dose for 3-month administration, 93% (39/42) of subjects and for LUPRON DEPOT-PED 30 mg dose for 3-month administration 100% (42/42) of subjects had sex steroid (estradiol or testosterone) suppressed to prepubertal levels at all visits.
* Clinical suppression of puberty in female patients was observed in 29 of 32 (90.6%) and 28 of 34 (82.4%) of patients in the 11.25 mg and 30 mg groups, respectively, at month 6.
* Clinical suppression of puberty in males was observed in 1 of 2 (50.0%) and 2 of 5 (40.0%) patients in the
11.25 mg and 30 mg groups, respectively, at month 6.
* In subjects with complete data for bone age, 29 of 33 (87.9 %) in the 11.25 mg group and 30 of 40 in the 30 mg group (75.0% ) had a decrease in the ratio of bone age to chronological age at month 6 compared to screening.

For additional information on this topic, please contact AbbVie Medical Information ([www.abbviemedinfo.com](http://www.abbviemedinfo.com)).

**Clinical Consideration: Patient is currently taking Lupron Depot-PED and needs to continue therapy until the appropriate time to resume normal puberty**

* LUPRON DEPOT-PED is indicated in the treatment of children with central precocious puberty (CPP).
* LUPRON DEPOT-PED should be discontinued at the appropriate age of onset of puberty at the discretion of the physician.
* Patient has not experienced hypersensitivity to GnRH, GnRH agonists or any of the excipients in LUPRON
DEPOT-PED, and is not pregnant or planning to become pregnant.

**LUPRON DEPOT-PED 7.5 mg, 11.25 mg, or 15 mg for 1-month administration**

* In an open-label study, 55 CPP subjects (49 females and 6 males, naïve to previous GnRHa treatment), were treated with LUPRON DEPOT-PED 1-month formulations until age appropriate for entry into puberty.
* The mean ± SD age at the start of treatment was 7 ± 2 years and the duration of treatment was 4 ± 2 years.
* The following effects have been noted with the chronic administration of leuprolide: cessation of menses (in girls), normalization and stabilization of linear growth and bone age advancement, stabilization of clinical signs and symptoms of puberty.

**LUPRON DEPOT-PED 11.25 mg or 30 mg for 3-month administration**

* The percentage of overall subjects with suppression of peak-stimulated LH to < 4.0 mIU/mL, as determined by assessments at months 2, 3 and 6 is 78.6% in the 11.25 mg dose and 95.2 in the 30 mg dose.

For additional information on this topic, please contact AbbVie Medical Information ([www.abbviemedinfo.com](http://www.abbviemedinfo.com)).

If I can provide any additional information, please contact me at <VARIABLE PHONE/FAX NUMBER> to ensure the prompt approval of this course of treatment.

Regards,

<VARIABLE PHYSICIAN NAME>

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