

LUPRON DEPOT-PED[®]

(leuprolide acetate for depot suspension)

Medical Necessity Letter

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Please see Important Safety Information on page 2.

Please visit <https://www.rxabbvie.com/pdf/lupronpediatric.pdf> for full Prescribing Information.

INDICATION¹

Central Precocious Puberty

LUPRON DEPOT-PED® (leuprolide acetate for depot suspension) 7.5 mg, 11.25 mg, and 15 mg for 1-month, 11.25 mg and 30 mg for 3-month, and 45 mg for 6-month administration are indicated for the treatment of pediatric patients with central precocious puberty (CPP).

IMPORTANT SAFETY INFORMATION¹

CONTRAINDICATIONS

- Hypersensitivity to gonadotropin-releasing hormone (GnRH), GnRH agonists, or any of the excipients in LUPRON DEPOT-PED. Anaphylactic reactions to synthetic GnRH or GnRH agonists have been reported.
- Pregnancy: LUPRON DEPOT-PED may cause fetal harm.

WARNINGS AND PRECAUTIONS

Initial Rise of Gonadotropins and Sex Steroid Levels

- During the early phase of therapy or after subsequent doses, gonadotropins and sex steroids may rise above baseline because of the initial stimulatory effect of the drug. Therefore, an increase in clinical signs and symptoms of puberty, including vaginal bleeding, may be observed during the first weeks of therapy or after subsequent doses.

Psychiatric Events

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

Convulsions

- 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.

Pseudotumor Cerebri (Idiopathic Intracranial Hypertension)

- Pseudotumor cerebri (idiopathic intracranial hypertension) have been reported in pediatric patients receiving GnRH agonists, including LUPRON DEPOT-PED. Monitor patients for signs and symptoms of pseudotumor cerebri, including headache, papilledema, blurred vision, diplopia, loss of vision, pain behind the eye or pain with eye movement, tinnitus, dizziness, and nausea.

ADVERSE REACTIONS

- The most common ($\geq 2\%$) adverse reactions in clinical studies with LUPRON DEPOT-PED 7.5 mg, 11.25 mg, and 15 mg for 1-month administration were: injection site reactions including abscess, emotional lability, acne/seborrhea, vaginitis/vaginal bleeding/vaginal discharge, pain, rash including erythema multiforme, headache, and vasodilation.
- The most common ($\geq 2\%$) adverse reactions in clinical studies with LUPRON DEPOT-PED 11.25 mg and 30 mg for 3-month administration were: injection site pain, increased weight, headache, altered mood, and injection site swelling.
- The most common ($\geq 4\%$) adverse reactions in clinical studies with LUPRON DEPOT-PED 45 mg for 6-month administration were: injection site reactions, headache, psychiatric events, abdominal pain, diarrhea, hemorrhage, nausea and vomiting, pyrexia, pruritus, pain in extremities, rash, back pain, ligament sprain, increased weight, fracture, breast tenderness, insomnia, chest pain, and hyperhidrosis.
- Diagnostic tests of pituitary gonadotropic and gonadal functions conducted during treatment and up to 6 months after discontinuation may be affected.
- The safety and effectiveness of LUPRON DEPOT-PED have not been established in pediatric patients less than 1 year old.
- LUPRON DEPOT-PED must be administered by a healthcare professional.

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 (include only one)

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

LUPRON DEPOT-PED is indicated for the treatment of pediatric patients 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.

Include only the data below that correspond to your requested dosing option (1-month, 3-month, or 6-month).

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 patients by month 1.
- In females, suppression of breast development ranged from 66.7% to 90.6% of patients 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 patients 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.
- 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 z-score changed from 1.6 at baseline to 0.7 at the end of the treatment phase.

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

- The percentage of overall patients 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 patients 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 patients and for LUPRON DEPOT-PED 30 mg dose for 3-month administration, 100% (42/42) of patients 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 patients 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.

LUPRON DEPOT-PED 45 mg for 6-month administration

- Suppression of peak-stimulated LH to < 4.0 mIU/mL at Week 24 was achieved in 39 of 45 (86.7%) patients overall.
- Suppression of peak-stimulated LH to < 4.0 mIU/mL at Week 24 was achieved in 22 of 27 (81.5%) treatment-naïve patients.
- The proportion of female patients with suppression of basal estradiol to <20 pg/mL was 97.4% at Week 24 and 100% at Week 48.
- The proportion of male patients with suppression of testosterone to <30 ng/dL was 100% at Weeks 24 and 48.
- Suppression (defined as regression or no change) of the physical signs of puberty was achieved in most patients.
- In patients with complete data for bone age, 40 of 45 (88.9%) and 42 of 45 (93.3%) had a decrease in the ratio of bone age to chronological age at Weeks 24 and 48, respectively, compared to baseline.

For additional information on this topic, please contact AbbVie Medical Information (www.abbviemedinfo.com).

Clinical Consideration: Patient treatment intolerance or previous treatment failure

LUPRON DEPOT-PED is indicated for the treatment of pediatric patients 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.

Include only the data below that correspond to your requested dosing option (3-month or 6-month).

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

- The percentage of overall patients 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 patients 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 patients and for LUPRON DEPOT-PED 30 mg dose for 3-month administration, 100% (42/42) of patients 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%) and 2 of 5 (40%) patients in the 11.25 mg and 30 mg groups, respectively, at month 6.
- In patients with complete data for bone age, 29 of 33 (88%) in the 11.25 mg group and 30 of 40 in the 30 mg group (75%) had a decrease in the ratio of bone age to chronological age at month 6 compared to screening.

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LUPRON DEPOT-PED 45 mg for 6-month administration

- Suppression of peak-stimulated LH to < 4.0 mIU/mL at Week 24 was achieved in 39 of 45 (86.7%) patients overall.
- Suppression of peak-stimulated LH to < 4.0 mIU/mL at Week 24 was achieved in 17 of 18 (94.4%) treatment-experienced patients.
- The proportion of female patients with suppression of basal estradiol to <20 pg/mL was 97.4% at Week 24 and 100% at Week 48.
- The proportion of male patients with suppression of testosterone to <30 ng/dL was 100% at Weeks 24 and 48.
- Suppression (defined as regression or no change) of the physical signs of puberty was achieved in most patients.
- In patients with complete data for bone age, 40 of 45 (88.9%) and 42 of 45 (93.3%) had a decrease in the ratio of bone age to chronological age at Weeks 24 and 48, respectively, compared to baseline.

For additional information on this topic, please contact AbbVie Medical Information (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 for the treatment of pediatric patients 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.

Include only the data below that correspond to your requested dosing option (1-month, 3-month, or 6-month).

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

- In an open-label study, 55 CPP patients (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 \pm 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 patients 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.

LUPRON DEPOT-PED 45 mg for 6-month administration

- Suppression of peak-stimulated LH to < 4.0 mIU/mL at Week 24 was achieved in 39 of 45 (86.7%) patients overall.
- Suppression (defined as regression or no change) of the physical signs of puberty was achieved in most patients.

For additional information this topic, please contact AbbVie Medical Information (www.abbviemedinfo.com).

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

Regards,

<VARIABLE PHYSICIAN NAME>

Reference: LUPRON DEPOT-PED [package insert]. North Chicago, IL: AbbVie Inc.

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