LUPRON DEPOT-PED 45 mg for 6 months

Prepared and edited on behalf of the PES Drug & Therapeutics committee: Shilpa Mehta, MD, Amit Lahoti, MD, Aditi Khokar, MD, Anna Ryabets-Lienhard, DO, and Ryan Miller, MD

LUPRON DEPOT-PED® (leuprolide acetate for depot suspension) 45 mg for 6-month intramuscular injection was approved for treatment of children with central precocious puberty (CPP). This approval adds a new option for management of CPP along with the previously available formulations including Lupron Depot-Ped monthly and 3-month intramuscular injections, Triptodur (triptorelin) 6-month intramuscular injection, Fensolvi (leuprolide acetate) 6-month subcutaneous injection and Supprelin (histrelin acetate) once yearly subcutaneous implant. The approval was based on the results of an open-label, single-arm, multicenter trial sponsored by AbbVie that assessed efficacy in 45 pediatric patients ages 4 to 10 years with CPP; 27 patients were naïve to GnRH agonist (GnRHa) therapy (24 females) and 18 previously treated (17 females). The study period was 48 weeks. The primary study endpoint of **peak stimulated LH <4.0 mIU/mL** at 24 weeks was achieved in 81.5% of the treatment-naive patients and 94.4% of previously treated patients (overall 86.7% of patients). Persistent LH suppression throughout the duration of the study and at 48 weeks was demonstrated in 92.6% of treatment naïve patients and 83.3% of previously treated patients (overall 88.9 % of patients)

In females, suppression of basal estradiol levels below 20 pg/mL was seen in over 97% patients at week 24 and week 48. Suppression of breast development in over 92% at week 24.
In males, suppression of testosterone below 30 ng/dL was seen in 100% (4/4) at weeks 24 and 48. Fifty percent of boys (n=2/4) at week 24 and 75 % (n=3/4) at week 48 showed suppression of genital development.

Mean height velocity in treatment-naive patients at baseline was 10.2 cm/year and decreased to 6.6 cm/year at week 24 and 6.7 cm/year at week 48. Mean height velocity in previously treated patients at baseline was 5.8 cm/year and decreased to 5.1 cm/year at week 24 and 5.3 cm/year at week 48.

Ratio of Bone age to Chronological Age decreased compared to baseline in over 88% subjects.

Adverse reactions reported in ≥ 4% of patient's included injection site reactions (78%), headache (33%), psychiatric events (22%), abdominal pain (18%), diarrhea (16%), hemorrhage (13%), nausea and vomiting (13%), pyrexia (13%), pruritus (11%), pain extremity (9%), back pain, ligament sprain, weight increase, fracture (7% each), breast tenderness, insomnia, chest and hyperhidrosis (4% each). No patients discontinued the treatment due to adverse reactions in this clinical trial.

LUPRON DEPOT-PED 45 mg 6-month intramuscular injection has the same administration and features as 3-month and 1-month Lupron doses (prefilled dual chamber syringe along with Lupraloc safety technology/ 23-gauge 1.5-inch needle and injection volume of 1.5 ml; no refrigeration is required). Contraindications include hypersensitivity to GnRH and pregnancy. The safety information provided by AbbVie for this formulation is same as the other Lupron preparations, including transient rise and worsening of pubertal development after initial

administration, psychiatric events during treatment, convulsion warning in patients with seizure disorders or CNS anomalies, and pseudotumor cerebri (for more information refer to FDA packet insert) (2). No head-to-head comparison studies with other GnRHa preparations are available to compare outcomes at this time.

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Reference:

1) https://classic.clinicaltrials.gov/ct2/show/results/NCT03695237
2) https://www.fda.gov/media/159663/download
3) Klein KO, et al. Efficacy and Safety of Leuprolide Acetate 6-Month Depot for the Treatment of Central Precocious Puberty: A Phase 3 Study. *Journal of the Endocrine Society*, Volume 7, Issue 7, July 2023, bvad071, https://doi.org/10.1210/jendso/bvad071

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