AETNA BETTER HEALTH®
Coverage Policy/Guideline

Name:	Leuprolide	Page:	1 of 5
Effective Date:	10/15/2025	Last Review Date:	9/2025

Applies to:	☒Illinois	☐Florida	☒Florida Kids
	☒New Jersey	☒Maryland	☐Michigan
	☒Pennsylvania Kids	☒Virginia	☐Kentucky PRMD

Intent:

The intent of this policy/guideline is to provide information to the prescribing practitioner outlining the coverage criteria for leuprolide under the patient's prescription drug benefit.

Description:

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications[1]

Leuprolide acetate is indicated in the palliative treatment of advanced prostate cancer.

Compendial Uses

- Central precocious puberty (CPP)[2-7,17]
- Use as a stimulation test to confirm the diagnosis of CPP[3-6]
- Use in combination with growth hormone for children with growth failure and advancing puberty[8-12]
- Prostate cancer[13]
- Inhibition of premature luteinizing hormone (LH) surges in members undergoing ovulation induction or assisted reproductive technology[14,15]
- Triggering of oocyte maturation and ovulation in assisted reproductive technology cycle[16]

All other indications are considered experimental/investigational and not medically necessary.

Applicable Drug List:

leuprolide acetate 1mg/0.2mL

Policy/Guideline:

Documentation

Submission of the following information is necessary to initiate the prior authorization review for central precocious puberty: laboratory report or medical record of a pubertal response to a gonadotropin releasing hormone (GnRH) agonist test or a pubertal level of a third-generation luteinizing hormone (LH) assay.

Coverage Criteria

Central Precocious Puberty (CPP)[2-7,17]

Authorization of 12 months may be granted for treatment of CPP when all of the following criteria are met:

- The diagnosis of CPP has been confirmed by a pubertal response to a gonadotropin releasing hormone (GnRH) agonist test or a pubertal level of a third-generation luteinizing hormone (LH) assay.
- The assessment of bone age versus chronological age supports the diagnosis of CPP.
- The member meets either of the following criteria:
    - The member is a female and was less than 8 years of age at the onset of secondary sexual characteristics.
    - The member is a male and was less than 9 years of age at the onset of secondary sexual characteristics.
- The pathologic cause of CPP has been assessed (e.g., imaging screening for intracranial tumors, genetic testing for familial CPP [e.g., MKRN3 or DLK1 mutations]).

Stimulation Test for CPP Diagnosis[3-6,17]

Authorization of one dose may be granted for use as a stimulation test to confirm the diagnosis of CPP.

Advancing Puberty and Growth Failure[8-12]

Authorization of 12 months may be granted for treatment of advancing puberty and growth failure in a pediatric member when leuprolide acetate is used in combination with growth hormone.

Prostate Cancer[1,13]

Authorization of 12 months may be granted for treatment of prostate cancer.

Inhibition of Premature Luteinizing Hormone (LH) Surges‡[14,15]

Authorization of 12 months may be granted for the inhibition of premature LH surges in members undergoing ovulation induction or assisted reproductive technology (ART).

Oocyte Maturation and Ovulation Trigger‡[16,18]

Authorization of 12 months may be granted for members undergoing ovulation induction or assisted reproductive technology (ART).

‡ Specialty Guideline Management coverage review will be bypassed for leuprolide if it is being requested for a procedure that has been approved under a member's medical benefit plan. Such members will be exempt from the requirements listed in the coverage criteria. A medical authorization number and confirmation of the approved procedure(s) will be required. NOTE: Some plans may opt-out of medical benefit alignment. Members receiving coverage under such plans must meet the requirements listed in the coverage criteria.

Continuation of Therapy

Central Precocious Puberty[2-7,17]

Authorization of up to 12 months may be granted for continued treatment for CPP when the member meets all of the following criteria:

- The member is currently receiving the requested medication through a paid pharmacy or medical benefit.
- The member is either a female less than 12 years of age or a male less than 13 years of age.
- The member is not experiencing treatment failure (e.g., clinical pubertal progression, lack of growth deceleration, continued excessive bone age advancement).

Prostate Cancer

Authorization of 12 months may be granted for continued treatment of prostate cancer in members requesting authorization who are experiencing clinical benefit to therapy (e.g., serum testosterone less than 50 ng/dL) and who have not experienced an unacceptable toxicity.

All Other Indications

All members (including new members) requesting authorization for continuation of therapy must meet all requirements in the coverage criteria.

Approval Duration and Quantity Restrictions:

Approval for Stimulation Test for CPP Diagnosis: One time

Approval for other indications: 12 months

References:

1. Leuprolide acetate injection [package insert]. Bridgewater, NJ: Amneal Pharmaceuticals LLC; February 2025.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2025. URL: http://www.clinicalpharmacology.com. Accessed May 15, 2025.
3. Carel J, Eugster EA, Rogol A, et al. Consensus statement on the use of gonadotropin-releasing hormone analogs in children. Pediatrics. 2009;123:e752-e762.
4. Bangalore Krishna K, Fuqua JS, Rogol AD, et al. Use of gonadotropin-releasing hormone analogs in children: Update by an international consortium. Horm Res Paediatr. 2019;91(6):357-372.
5. Kletter GB, Klein KO, Wong YY. A pediatrician's guide to central precocious puberty. Clin Pediatr. 2015;54:414-424.
6. Bangalore Krishna K, Silverman LA. Diagnosis of central precocious puberty. Endocrinol Metab Clin North Am. 2024;53(2):217-227.
7. Kaplowitz P, Bloch C, the Section on Endocrinology. Evaluation and referral of children with signs of early puberty. Pediatrics. 2016;137:e20153732.
8. Kamp GA, Mul D, Waelkens JJ, et al. A randomized controlled trial of three years growth hormone and gonadotropin-releasing hormone agonist treatment in children with idiopathic short stature and intrauterine growth retardation. J Clin Endocrinol Metab. 2001;86:2969-2975.
9. Mericq V, Cajardo H, Effers M, et al. Effects of treatment with GH alone or in combination with LHRH analog on bone mineral density in pubertal GH-deficient patients. J Clin Endocrinol Metab. 2002;87:84-89.
10. Mul D, Wit JM, Oostdijk W, et al. The effect of pubertal delay by GnRH agonist in GH-deficient children on final height. J Clin Endocrinol Metab. 2001;86:4655-4656.
11. Quintos JB, Vogiatzi MG, Harbison MD, et al. Growth hormone therapy alone or in combination with gonadotropin-releasing hormone analog therapy to improve the height deficit in children with congenital adrenal hyperplasia. J Clin Endocrinol Metab. 2001;86:1511-1517.
12. Tanaka T, Satoh M, Yasunaga T, et al. GH and GnRH analog treatment in children who enter puberty at short stature. J Pediatr Endocrinol Metab. 1997;10:623-628.
13. The NCCN Drugs & Biologics Compendium® © 2025 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed May 20, 2025.
14. Urman B, Yakin K. Ovulatory disorders and infertility. J Reprod Med. 2006;51(4):267-282.
15. National Institute for Health and Clinical Excellence (NICE). Guideline on assessment and treatment for people with fertility problems. NICE 2017 Feb 6:CG156.
16. Casper RF. Reducing the Risk of OHSS by GnRH Agonist Triggering. J Clin Endocrinol Metab. 2015;100(12):4396-8.
17. Cheuiche AV, da Silveira LG, de Paula LCP, et al. Diagnosis and management of precocious sexual maturation: an updated review. Eur J Pediatr. 2021;180(10):3073-3087.
18. Practice Committee of the American Society for Reproductive Medicine. Prevention and treatment of moderate and severe ovarian hyperstimulation syndrome: a guideline. Fertil & Steril. 2016. 106(7):1634-1647.
19. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Head and Neck Cancers. Version 2.2024. Accessed February 15, 2024. https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf.

20. Popovic J, Geffner ME, Rogol AD, et al. Gonadotropin-releasing hormone analog therapies for children with central precocious puberty in the United States. Front Pediatr. 2022;10:968485. doi:10.3389/fped.2022.968485