AETNA BETTER HEALTH®
Coverage Policy/Guideline

Name:	Leuprolide	Page:	1 of 5
Effective Date:	11/1/2024	Last Review Date:	10/2024

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.

A. FDA-Approved Indication
Leuprolide acetate is indicated in the palliative treatment of advanced prostate cancer.

B. Compendial Uses
1. Central precocious puberty (CPP)
2. Use as a stimulation test to confirm the diagnosis of CPP
3. Use in combination with growth hormone for children with growth failure and advancing puberty
4. Prostate cancer
5. Inhibition of premature luteinizing hormone (LH) surges in members undergoing ovulation induction or assisted reproductive technology
6. Androgen receptor positive salivary gland tumors
7. Triggering of oocyte maturation and ovulation in assisted reproductive technology cycle

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.

Criteria for Initial Approval:

A. Central precocious puberty (CPP)

1. Authorization of 12 months may be granted for treatment of CPP in a female member when all of the following criteria are met:
   i. Intracranial tumor has been evaluated by appropriate lab tests and diagnostic imaging (e.g., computed tomography [CT] scan, magnetic resonance imaging [MRI]).
   ii. 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.
   iii. The assessment of bone age versus chronological age supports the diagnosis of CPP.
   iv. The member was less than 8 years of age at the onset of secondary sexual characteristics.
2. Authorization of 12 months may be granted for treatment of CPP in a male member when all of the following criteria are met:
   i. Intracranial tumor has been evaluated by appropriate lab tests and diagnostic imaging (e.g., CT scan, MRI).
   ii. The diagnosis of CPP has been confirmed by a pubertal response to a GnRH agonist test or a pubertal level of a third-generation LH assay.
   iii. The assessment of bone age versus chronological age supports the diagnosis of CPP.
   iv. The member was less than 9 years of age at the onset of secondary sexual characteristics.

B. Stimulation test for CPP diagnosis

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

C. Advancing puberty and growth failure

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.

D. Prostate cancer

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

E. Salivary gland tumors

Authorization of 12 months may be granted for treatment of recurrent, unresectable or metastatic salivary gland tumors as a single agent when the tumor is androgen receptor positive.

Continuation of Therapy:

A. Central precocious puberty

1. Authorization of up to 12 months may be granted for continuation of therapy for CPP in a female member if the member is currently less than 12 years of age and the member meets both of the following:
   i. The member is currently receiving the requested medication through a paid pharmacy or medical benefit.
   ii. The member is not experiencing treatment failure (e.g., clinical pubertal progression, lack of growth deceleration, continued excessive bone age advancement).
2. Authorization of up to 12 months may be granted for continuation of therapy for CPP in a male member if the member is currently less than 13 years of age and the member meets both of the following:
   i. The member is currently receiving the requested medication through a paid pharmacy or medical benefit.
   ii. The member is not experiencing treatment failure (e.g., clinical pubertal progression, lack of growth deceleration, continued excessive bone age advancement).

B. Salivary gland tumors

Authorization of 12 months may be granted for continued treatment of salivary gland tumors in members requesting authorization who are experiencing clinical benefit to therapy and who have not experienced an unacceptable toxicity.

C. 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.

D. All other indications

All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

Approval Duration and Quantity Restrictions:

Approval: 12 months

References:

1. Leuprolide acetate injection [package insert]. Bridgewater, NJ: Amneal Pharmaceuticals LLC; March 2023.
2. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2024. URL: http://www.clinicalpharmacology.com. Accessed February 13,2024.
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. Houk CP, Kunselman AR, Lee PA. Adequacy of a single unstimulated luteinizing hormone level to diagnose central precocious puberty in girls. *Pediatrics*. 2009;123:e1059-e1063.
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® © 2024 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed February 13, 2024.
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.