Effective date: 5/2019
Last Reviewed: 2/2020, 5/2021, 4/2022, 5/2023 Scope: Medicaid

NON-ONCOLOGY POLICY
leuprolide acetate injection

For oncology indications, please refer to NHPRI LHRH agonists and antagonist Oncology Policy

I. NON-ONCOLOGY INDICATIONS

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 Indications

1. Central precocious puberty (CPP): Leuprolide acetate is indicated in the treatment of children with central precocious puberty.

B. Compendial Uses
1. Use as a stimulation test to confirm the diagnosis of CPP
2. Use in combination with growth hormone for children with growth failure and advancing puberty
3. Gender dysphoria (also known as gender non-conforming or transgender persons)

All other indications are considered experimental/investigational and are not a covered benefit.

II. CRITERIA FOR INITIAL APPROVAL

A. Central precocious puberty (CPP)
1. Authorization up to age 12 may be granted for the treatment of CPP in a female member when all of the following criteria are met:
   a. 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.
   b. The assessment of bone age versus chronological age supports the diagnosis of CPP.
   c. The member was less than 8 years of age at the onset of secondary sexual characteristics.
2. Authorization up to age 13 may be granted for the treatment of CPP in a male member when all of the following criteria are met:
   a. 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.
   b. The assessment of bone age versus chronological age supports the diagnosis of CPP.
   c. 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 the treatment of advancing puberty and growth failure in a pediatric member when leuprolide acetate is used in combination with growth hormone.

D. Gender dysphoria
Authorization of 12 months may be granted for pubertal suppression in preparation for gender reassignment when all of the following are met:

1. Patient has a diagnosis of gender dysphoria as confirmed by a qualified mental health professional (MHP)****** OR the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V) Criteria §; **AND**
2. A qualified MHP****** has confirmed all of the following:
    a. Patient has demonstrated a long-lasting and intense pattern of gender nonconformity or gender dysphoria (whether suppressed or expressed); **AND**
    b. Gender dysphoria worsened with the onset of puberty; **AND**
    c. Any coexisting psychological, medical, or social problems that could interfere with treatment (e.g., that may compromise treatment adherence) have been addressed, such that the adolescent's situation and functioning are stable enough to start treatment; **AND**
    d. Patient has sufficient mental capacity to give informed consent to this (reversible) treatment; **AND**
3. Patient has been informed of the effects and side effects of treatment (including potential loss of fertility if the individual subsequently continues with sex hormone treatment) and options to preserve fertility; **AND**
4. Patient has given informed consent and (particularly when the adolescent has not reached the age of legal medical consent, depending on applicable legislation) the parents or other caretakers or guardians have consented to the treatment and are involved in supporting the adolescent throughout the treatment process; **AND**
5. A pediatric endocrinologist or other clinician experienced in pubertal assessment has confirmed all of the following:
    a. Agreement in the indication for treatment; **AND**
    b. Puberty has started in the adolescent (e.g., Tanner stage ≥G2/B2); **AND**

c. There are no medical contraindications to treatment

III. CONTINUATION OF THERAPY

A. Central precocious puberty

1. Authorization up to age 12 may be granted for continuation of therapy for CPP in a female member if the member is currently less than 12 years of age.
2. Authorization up to age 13 may be granted for continuation of therapy for CPP in a male member if the member is currently less than 13 years of age.

B. Gender Dysphoria

Authorization of 12 months if patient has shown a beneficial response to treatment as evidenced by routine monitoring of clinical pubertal development and applicable laboratory parameters.

C. Stimulation test for CPP diagnosis and advancing puberty and growth failure

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

**** Definition of a qualified mental health professional**

- A master's degree or its equivalent in a clinical behavioral science field. This degree or a more advanced one should be granted by an institution accredited by the appropriate national or regional accrediting board. The mental health professional should also have documented credentials from the relevant licensing board or equivalent; **AND**
- Competence in using the Diagnostic Statistical Manual of Mental Disorders and/or the International Classification of Diseases for diagnostic purposes; **AND**
- Ability to recognize and diagnose co-existing mental health concerns and to distinguish these from gender dysphoria; **AND**
- Knowledgeable about gender nonconforming identities and expressions, and the assessment and treatment of gender dysphoria; **AND**

Continuing education in the assessment and treatment of gender dysphoria. This may include attending relevant professional meetings, workshops, or seminars; obtaining supervision from a mental health professional with relevant experience; or participating in research related to gender nonconformity and gender dysphoria.

§ DSM-V Criteria for Gender Dysphoria

- A marked incongruence between one's experienced/expressed gender and natal gender of at least 6mo in duration, as manifested by at least TWO of the following:
  - A marked incongruence between one's experienced/expressed gender and primary and/or secondary sex characteristics (or in young adolescents, the anticipated secondary sex characteristics)
  - A strong desire to be rid of one's primary and/or secondary sex characteristics because of a marked incongruence with one's experienced/expressed gender (or in young adolescents, a desire to prevent the development of the anticipated secondary sex characteristics)

- A strong desire for the primary and/or secondary sex characteristics of the other gender
- A strong desire to be of the other gender (or some alternative gender different from one's designated gender)
- A strong desire to be treated as the other gender (or some alternative gender different from one's designated gender)
- A strong conviction that one has the typical feelings and reactions of the other gender (or some alternative gender different from one's designated gender); **AND**

- The condition is associated with clinically significant distress or impairment in social, occupational, or other important areas of functioning; **AND**
- Specify one of the following:
  - The condition exists with a disorder of sex development; **OR**

The condition is post-transitional, in that the individual has transitioned to full-time living in the desired gender (with or without legalization of gender change) and has undergone (or is preparing to have) at least one sex-related medical procedure or treatment regimen—namely, regular sex hormone treatment or gender reassignment surgery confirming the desired gender (e.g., penectomy, vaginoplasty in natal males; mastectomy or phalloplasty in natal females).

IV. REFERENCES

1. Leuprolide acetate injection [package insert]. Princeton, NJ: Sandoz Inc.; March 2023.
2. Lupron injection for pediatric use [package insert]. North Chicago, IL: Abbvie Inc.; February 2021.
3. Micromedex (electronic version). Truven Health Analytics, Greenwood Village, CO. Available at: http://www.micromedexsolutions.com Accessed January 8, 2019.
4. 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.
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. National Collaborating Centre for Women's and Children's Health. Fertility: assessment and treatment for people with fertility problems (Clinical guideline no. 156). National Institute for Health and Clinical Excellence (NICE); 2013.