Pharmacy Policy Bulletin: J-1206 Gonadotropin-Releasing Hormone (GnRH) Agonists – Commercial and Healthcare Reform	
Number: J-1206	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Injectable = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-1206-006	**Original Date:** 04/06/2022
Effective Date: 07/18/2025	**Review Date:** 06/25/2025

Drugs Product(s):	• Leuprolide acetate depot suspension • Lupron Depot (leuprolide acetate for depot suspension) • Lupron Depot-Ped (leuprolide acetate for depot suspension) • Lutrate Depot (leuprolide acetate for depot suspension)

FDA-Approved Indication(s):	• Leuprolide acetate depot 22.5 mg, Lutrate Depot
	  ○ Treatment of advanced prostatic cancer.
	• Lupron Depot 3.75 mg, 11.25 mg
	  ○ Management of endometriosis, including pain relief and reduction of endometriotic lesions.
	  ○ In combination with a norethindrone acetate for initial management of the painful symptoms of endometriosis and for management of recurrence of symptoms.
	  ○ Concomitant use with iron therapy for preoperative hematologic improvement of women with anemia caused by uterine leiomyomata (fibroids) for whom three months of hormonal suppression is deemed necessary.
	• Lupron Depot 7.5 mg, 22.5 mg, 30 mg, 45 mg
	  ○ Palliative treatment of advanced prostatic cancer.
	• Lupron Depot-Ped
	  ○ Treatment of pediatric patients with central precocious puberty (CPP).

Background:	• Gonadotropin-releasing hormone (GnRH) agonists act as inhibitors of gonadotropin secretion. Administration results in inhibition of the growth of certain hormone-dependent tumors. • **Prostate Cancer** ○ National Comprehensive Cancer Network (NCCN) guidelines do not differentiate between the leuprolide products for the treatment of prostate cancer.

- **CPP**
    - CPP is a condition that causes early sexual development in females and males. While puberty normally starts between ages 8 and 13 in females and between ages 9 and 14 in males, females with CPP begin exhibiting signs before age 8 and males before age 9, and is accompanied by significant advancement of bone age.
    - The diagnosis should be confirmed by pubertal gonadal sex steroid levels and a pubertal luteinizing hormone (LH) response to stimulation by native GnRH. CPP is characterized by basal LH concentrations > 0.2 to 0.3 international units per liter (IU/L) and/or stimulated LH concentration post-GnRH or GnRH agonist of > 3.3 to 5.0 IU/L.
    - Magnetic resonance imaging or CT-scanning of the brain is recommended to detect hypothalamic or pituitary tumors, or anatomical changes associated with increased intracranial pressure. Other causes of sexual precocity, such as congenital adrenal hyperplasia, testotoxicosis, testicular tumors and/or other autonomous feminizing or masculinizing disorders must be excluded by proper clinical hormonal and diagnostic imaging examinations.
    - Bone age is the degree of maturation of a child's bones, and is measured by taking an X-ray of the left wrist, hand, and fingers. In CPP, a child's bone age is advanced beyond their chronological age due to linear growth acceleration and acceleration of bone maturation, which can lead to short adult height.
    - Efficacy assessments in CPP include the suppression of gonadotropins (luteinizing hormone and follicle stimulating hormone) and gonadal sex steroids (estrogen in girls and testosterone in boys, respectively) during pharmacologic treatment.
- **Gender Dysphoria**
    - The Gender Dysphoria/Gender Incongruence Guidelines from the Endocrine Society recommend that, where indicated, GnRH analogues are used to suppress pubertal hormones in adolescents. A benefit of pubertal suppression at early puberty may be a better psychological and physical outcome. Treating gender dysphoria/gender-incongruent adolescents entering puberty with GnRH analogs has been shown to improve psychological functioning in several domains. An advantage of using GnRH analogs is the reversibility of the intervention. If, after extensive exploration of his/her transition wish, the individual no longer desires transition, they can discontinue pubertal suppression. Additionally, GnRH agonists are used in hormone regimens in transgender persons of adult age.
    - The Gender Dysphoria/Gender Incongruence Guidelines from the Endocrine Society acknowledge it may be appropriate to initiate treatment in adolescents under 16 years old. Adolescents under 16 years old should be treated by clinicians competent in the evaluation and induction of pubertal development. Clinicians with these competencies may include, but are not limited to pediatricians, family medicine physicians, and endocrinologists.
    - Prescribing gender affirming hormones is within the scope primary care physicians, obstetricians-gynecologists, endocrinologists, advanced practice nurses, and physician assistants. Depending on the practice setting and jurisdiction, other providers with prescriptive rights such as nurse midwives may also be appropriate to prescribe and manage this care.
- **Endometriosis**
- The American College of Obstetricians and Gynecologists lists first line therapy for pain associated with endometriosis as NSAIDs, other nonopioid analgesia,

	combined hormonal contraceptives, and progestins. Second line therapy includes GnRH agonists, progestin IUD, and danazol. Third line therapy includes surgery such as laparoscopy, laparotomy, interruption of nerve pathways, and hysterectomy and oophorectomy.ICD-10 Code Information: ○ ICD-10: E30.1 "Precocious puberty" may apply to Lupron Depot-Ped; however, the prescriber must confirm that the member has central precocious puberty. • Prescribing considerations: ○ Eligard provides continuous release of leuprolide over a 1-, 3-, 4-, or 6-month period. ○ Due to different release characteristics, the dosage strengths are not additive and must be selected based upon the desired dosing schedule.

Approval Criteria

I. Initial Authorization

A. Advanced Prostate Cancer

1. Leuprolide acetate depot 22.5 mg

When a benefit, leuprolide acetate depot may be approved when the following criterion is met **(a.)**:

a. The member has a diagnosis of advanced prostate cancer (ICD-10: C61).

2. Lupron Depot 7.5 mg, 22.5 mg, 30 mg, or 45 mg; Lutrate Depot

When a benefit, coverage of Lupron Depot 7.5 mg, 22.5 mg, 30 mg, or 45 mg, or Lutrate Depot, may be approved when all of the following criteria are met **(a. and b.)**:

a. The member has a diagnosis of advanced prostate cancer (ICD-10: C61).

b. The member has experienced therapeutic failure or intolerance to plan-preferred Eligard.

B. Central Precocious Puberty

When a benefit, coverage of Lupron Depot-Ped may be approved when all of the following criteria are met **(1. through 4.)**:

1. The member has a diagnosis of central precocious puberty (no ICD-10 code).

2. The member meets one (1) of the following criteria for the onset of secondary sexual characteristics **(a., b., or c.)**:

a. The member is less than 8 years of age if female.

b. The member is less than 9 years of age if male.

c. If age is greater than the above, the prescriber attests that therapy is medically necessary.

3. The member meets one (1) of the following criteria **(a. or b.)**:

a. The member has elevated basal luteinizing hormone (LH) level > 0.2 - 0.3 IU/L.

b. The member has elevated leuprolide-stimulated LH level > 3.3 – 5.0 IU/L.

4. The member has advancement of bone age beyond chronological age.

C. Endometriosis

When a benefit, coverage of Lupron Depot 3.75 mg or 11.25 mg may be approved when the following criterion is met **(1.)**:

1. The member has a diagnosis of endometriosis (ICD-10: N80.9).

D. Gender Dysphoria or Gender Identify Disorder

When a benefit, coverage of Lupron Depot or Lupron Depot-Ped may be approved when all of the following criteria are met **(1. and 2.)**:

1. The member has a diagnosis of gender dysphoria or gender identity disorder (ICD-10: F64).

2. If the member is 15 years of age or younger, the member meets the following criterion **(a.)**:
   a. The drug is prescribed by a clinician competent in the evaluation and induction of pubertal development.

E. Uterine Leiomyomata

When a benefit, coverage of Lupron Depot 3.75 mg or 11.25 mg may be approved when all of the following criteria are met **(1. and 2.)**:

1. The member has a diagnosis of uterine leiomyomata (ICD-10: D25).
2. The member will be using Lupron Depot concomitantly with iron therapy.

II. Reauthorization

A. Advanced Prostate Cancer, Endometriosis, Uterine Leiomyomata, or Gender Dysphoria/Gender Identify Disorder

When a benefit, reauthorization of leuprolide acetate depot, Lupron Depot, Lupron Depot-Ped, or Lutrate Depot may be approved when all of the following criteria are met **(1. and 2.)**:

1. The prescriber attests that the member has experienced a positive clinical response to therapy.
2. The member requires continued therapy with the requested product.

B. Central Precocious Puberty

When a benefit, reauthorization of Lupron Depot-Ped may be approved when the following criterion is met **(1.)**:

1. The member has experienced positive clinical response to therapy defined as one (1) of the following criteria **(a. through f.)**:
   a. Pre-pubertal slowing or decline
   b. Normalization of follicle stimulating hormone (FSH)
   c. Normalization of LH
   d. Normalization of bone age
   e. Normalization of estradiol level
   f. Normalization of testosterone level

III. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

IV. Coverage of oncology drug(s) listed in this policy may be approved on a case-by-case basis per indications supported in the most current NCCN guidelines.

Limitations of Coverage

I. Coverage of drug(s) addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.

II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR Plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None.

References:

1. Lupron Depot 7.5 mg, 22.5 mg, 30 mg, 45 mg [package Insert]. North Chicago, IL: AbbVie, Inc.; March 2024.
2. Lupron Depot 3.75 mg [package Insert]. North Chicago, IL: AbbVie, Inc.; January 2023.
3. Lupron Depot 11.25 mg [package Insert]. North Chicago, IL: AbbVie, Inc.; March 2020.
4. Eligard [package insert]. Fort Collins, CO: Tolmar, Inc.; May 2024.
5. Leuprolide acetate depot [package insert]. Warren, NJ: Cipla USA, Inc.; August 2024.
6. Lutrate depot [package insert]. Warren, NJ: Cipla USA, Inc.; February 2023.
7. NCCN Guidelines Version 4.2024. Prostate Cancer. National Comprehensive Cancer Network. Available at: https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed September 12, 2024.
8. Carel JC, Eugster EA, Rogol A, et al. Consensus Statement on the Use of Gonadotropin-Releasing Hormone Analogs in Children. *Pediatrics* 2009; 123: e752-e762.
9. UpToDate. Definition, etiology, and evaluation of precocious puberty. Accessed May 20, 2020.
10. Hembree WC, Cohen-Kettenis PT, Gooren L, et al. Endocrine Treatment of Gender-Dysphoric/Gender-Incongruent Persons: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2017;102(11):3869-3903.
11. Becker CM, Bokor A, Heikinheimo O, Horne A, Jansen F, Kiesel L, King K, Kvaskoff M, Nap A, Petersen K, Saridogan E, Tomassetti C, van Hanegem N, Vulliemoz N, Vermeulen N; ESHRE Endometriosis Guideline Group. ESHRE guideline: endometriosis. Hum Reprod Open. 2022 Feb 26;2022(2).